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ANOREXIA NERVOSA OR HYPOPITUITARISM?

HEINZ MAGENDANTZ, M.D.
AND
SAMUEL PROGER, M.D.
BOSTON

In the nebulous zone where endocrinology shades into psychiatry as at the climacteric, the puerperium and adolescence, no more elusive figure is to be encountered than the syndrome variously called anorexia nervosa, hypopituitarism or incipient Simmonds' disease.

The following example attempts to portray the experience of the clinician faced with this syndrome, one which is evidently appearing with greater frequency:

The patient is an adolescent girl whose mother states that the girl has been quite well until three months before, when she suddenly, for no apparent cause, completely lost her appetite. Since then the hitherto joyous child has become difficult, shy, restless, even sleepless. Coincident with this change in her personality there has been a progressive loss of weight until she now looks "like a skeleton draped in skin" and her chubby girlish features have changed into an awkward ugliness. Her menstrual periods have ceased, her soft, childlike skin has become dry and wrinkled. She shivers even in warm weather and will not leave the house in winter unless dressed in her warmest clothes. Her whole family has tried to coax her to eat with no success, the only result being tears and resentment on the part of the girl, who insists she just cannot eat and that even the sight of food nauseates her. Forcing food has caused vomiting. The mother was alarmed when she found remnants of food hidden in strange places, food which she supposed her daughter had eaten. Reproaches were of no avail. It seemed unbelievable that such a frail, emaciated person could not only live on a few sips of tea and milk and some fruit but even be on her feet all day, busy around the house and not visibly tired or weak.

Such is the mother's story. As to the daughter, she looks as though she were wasted away by a severe consumptive illness, all her ribs and pelvic bones being visible, her skin dry and cold, her pulse alarmingly slow, her blood pressure very low, her temperature subnormal; and yet careful examination reveals no other abnormality than the extreme emaciation. The patient, in a sullen, tense mood, insists that there is nothing wrong with her and asks only to be left alone.

What are we dealing with? A severe metabolic disorder? Advanced pulmonary tuberculosis? A psychosis? When the patient is placed under observation in a hospital it is discovered that her basal metabolic rate is astonishingly low, possibly as low as —40 per cent, that her heart rate per minute is in the forties, her fasting blood sugar between 60 and 70 mg. per hundred cubic centimeters, her dextrose tolerance curve of a peculiar flat, slowly rising type, her urine scanty but otherwise normal, her blood perhaps showing a moderate but not striking hypochromic anemia. All efforts to give her a high caloric diet are frustrated because she won't take the food; all tonics, iron and thyroid seem to be of no avail. Finally we consult a neuropsychiatrist, who studies her emotional life.

Does he succeed in getting at the root of the evil? Does the patient finally develop a fear of dying? Does the ugliness of her body stimulate her vanity? It is difficult to determine what overcomes her morbid dislike of food, but suddenly, maybe on a given day, she begins to eat, often ravenously. The change in her whole attitude is amazing. Half a year later her mother reports that her daughter is again her former self physically and mentally; that she has gained 40 pounds (18 Kg.), that her menstrual periods have become normal and that she now enjoys life and eats anything and everything. What brought about this miraculous cure?

Our purpose in this report is to present and discuss three such cases with this strange syndrome which were observed at the Diagnostic Hospital of the Boston Dispensary.

Almost 250 years ago Morton[1] described a few cases of such striking similarity to the picture just sketched that it seems reasonable to assume that he was dealing with the same disease. Translated, his salient sentences read as follows: "The atrophia or phthisis nervosa is a consumption of the body without any sign of fever, cough or dyspnea, but accompanied by an inversion of the appetite and the digestion until finally there results a feebleness and torpor of the whole body which increases from day to day." (Atrophia seu phthisis nervosa est consumptio corporis absque ulla insigni febre, vel tussi, vel dyspnoea; verum cum appetitus et digestionis eversione eam comitante: unde insequitur totius corporis languor et marcor indies increscens.)

As to etiology, he made the following remarks: "The constant cause of this disease seems to me to be of nervous nature, an unnatural state of the mind, originating from an inverted nervous tonus whence I am used to call it phthisis from its bodily aspect." (Causa continuens hujus morbi mihi videtur esse in genere nervosa, a praeternaturali statu spiritum animalium et a tono nervorum everso proveniens inde eam vocare soleo Phthisin in habitu corporis.)

Of one patient, an 18 year old girl, he says "I can't remember having ever seen in my whole practice any

From the Joseph H. Pratt Diagnostic Hospital.

1. Morton, Richard: Phthisiologia, seu exercitationes de phthisi, London, S. Smith, 1689.

living person reduced to such a state of marasmus, like a skeleton draped with skin." (Numquam aliquem ita marasmo confectum [sceleti instar cuti vestiti] adhuc viventem in toto praxi mea observatum memini.)

Another patient, a 16 year old boy who studied too much, "fell into almost total anorexia and then into universal atrophy." (Incidit in inappetentiam fere totalem et inde in atrophiam universalem.)

About a hundred years later, in 1873, Sir William Gull and Ernest Charles Lasègue reported their studies of patients with the same syndrome, giving it various names. Gull [2] used the expression anorexia nervosa (apepsia hysterica) and believed that the want of appetite was due to a morbid mental state. Discussing his paper, a physician told of a patient of his own who, as he put it, resembled a dried mummy more than a living being. In 1888 Gull [3] published the photographs of such an emaciated patient, who was a plump, healthy girl until she began, without apparent cause, to evince a repugnance to food. She insisted on walking to the office, though an object of remarks by the passers-by. Her respiratory rate was from 12 to 14 per minute, her pulse rate 46 per minute, her temperature 97 F., her weight 4 stone 7 (61 pounds, or 28 Kg.), her height 5 feet 4 inches (163 cm.). The photographs show the striking change after she became well again; she had no trouble at all and was eating everything. In Gull's opinion the cause lay in a perversion of the "ego." He was also impressed by the patient's persistent wish to be constantly on the move, even though the emaciation was so great. Lasègue,[4] in a fine character study of a hypothetic case with "hysterical anorexia," remarked that "we are defective in expressions for the degree or varieties of inappetence—the poverty of our vocabulary corresponding to the insufficiency of our knowledge." Concerning the strange attitude of these patients toward food, he said "I have seen one chewing morsels of rhubarb, whom no consideration would have induced to taste a cutlet." Stephens [5] was probably the first to report a fatal case with necropsy. The picture of this 16 year old girl is truly shocking. Her height was 5 feet 4 inches (163 cm.), her body weighed 49 pounds (22 Kg.); ten months previously she had been a remarkably well developed, plump and healthy looking girl. The body showed good teeth (an important fact in view of the cases of pituitary cachexia, or Simmonds' disease, which we shall discuss later), and there was not a trace of fat except in her breasts, which stood out boldly. The brain was normal throughout (no mention was made of the pituitary gland). The weights of the organs are interesting: heart 4 ounces (113 Gm.), liver 23½ ounces (666 Gm.), pancreas 1½ ounces (43 Gm.), spleen 1¼ ounces (35 Gm.), adrenals each one-fourth ounce (7 Gm.), and uterus and ovaries together seven-eighths ounce (25 Gm.).

In more recent times Déjerine and Gauckler [6] described cases of "mental anorexia." In their opinion this anorexia is of purely emotional origin. They found the cases to be extraordinarily numerous. They tried to differentiate between primary and secondary anorexia and stated that patients with "mental anorexia" might die of inanition. The therapeutic and prognostic difficulties in a syndrome of such doubtful etiology were admitted in the remark that there was absolutely no way of telling whether a patient would or would not respond to treatment.

Following these papers, full of keen observations and wise remarks, come the days of experimental medicine when endocrinology began to occupy the minds of many who were working on this special problem, until the psychologic side was in danger of being neglected.

Before Simmonds,[7] in a paper entitled "Pituitary Atrophy With Fatal Outcome," made his all important contribution, Falta [8] claimed to have made the diagnosis of pituitary dystrophia clinically, which was later confirmed by autopsy. The pathologist Simmonds [9] reported in several papers, dating from 1914, his observations on cases of what is now known as pituitary cachexia, or Simmonds' disease. According to him the disease (which now goes by his name) is characterized by chronic cachexia, senile appearance, wrinkled facial skin, breaking off of the teeth, disappearance of the menses, loss of axillary and pubic hair and striking diminution in the size of the inner organs (splanchnomicry). He associated these features with atrophy (fibrosis, necrosis) of the anterior lobe of the pituitary gland. He favored the embolic origin of the pituitary atrophy and pointed out that in three of his cases the disease began at the puerperium. However, he saw instances in which the pituitary atrophy had been brought about by a tumor pressing on the gland. It is important to note that Simmonds' patients were mostly women of child-bearing age; also that some of the characteristics he described, namely the breaking off of teeth and loss of axillary and pubic hair, are not mentioned among the detailed descriptions of the cases of anorexia nervosa. This suggests that Simmonds' disease and anorexia nervosa are not one and the same.

Before discussing this question, however, it would be well to mention some of the numerous articles following Simmonds' original publication, particularly some of the more recent ones, in which are analyzed nonfatal cases of what appeared to be either anorexia nervosa or pituitary cachexia. Moeller [10] gave a detailed report of his patients with anorexia nervosa who showed bradycardia, arterial hypotension, hypoglycemia, low basal metabolic rate, amenorrhea, hypertrichosis and obstipation. He discussed the influence of starvation on the function of endocrine glands. Graubner [11] collected thirty-three cases of pituitary cachexia from the literature and added one of his own. Zondek and Koehler [12] reported cases of cerebral-pituitary "magersucht," an untranslatable word meaning the contrary of obesity but with implied morbidity. Thannhauser [13] discussed the problem of "endogenous leanness" from a broad standpoint, coming to the conclusion that the body build was more important than the determination of oxygen consumption and specific dynamic action in differentiating the various types of endocrine leanness. He separated cases of leanness with thyroid, adrenal and

2. Gull, W. W.: Anorexia Nervosa, Tr. Clin. Soc. London **7**: 22, 1874; Meeting of the Clinical Society, M. Times & Gaz. **2**: 534, 1873.

3. Gull, William: Anorexia Nervosa, Lancet **1**: 516, 1888.

4. Lasègue, E. C.: On Hysterical Anorexia, M. Times & Gaz. **2**: 265, 1873.

5. Stephens, Lockhart: Case of Anorexia Nervosa: Necropsy, Lancet **1**: 31, 1895.

6. Déjerine, J., and Gauckler, E.: Les manifestations fonctionelles des psychoneuroses, Paris, Masson & Cie, 1911, p. 6.

7. Simmonds, Morris: Ueber Hypophysenschwund mit tödlichem Ausgang, Deutsche med. Wchnschr. **40**: 322, 1914.

8. Falta, W.: Die Erkrankungen der Blutdrüsen, Berlin, Julius Springer, 1913, p. 256.

9. Simmonds, Morris: Ueber Kachexie hypophysären Ursprungs, Deutsche med. Wchnschr. **42**: 190, 1916; Atrophie des Hypophysenvorderlappens und hypophysäre Kachexie, ibid. **44**: 852, 1918.

10. Moeller, E.: Quantitative Verhältnisse des Stoffwechsels bei Unterernährung, illustriert durch vier Fälle von nervöser Anorexie, Klin. Wchnschr. **3**: 1575, 1924.

11. Graubner, W.: Die hypophysäre Kachexie (Simmonds'sche Krankheit) Ztschr. f. klin. Med. **101**: 249, 1925.

12. Zondek, H., and Koehler, G.: Ueber zerebral-hypophysäre Magersucht, Deutsche med. Wchnschr. **54**: 1955 (Nov. 23) 1928.

13. Thannhauser, S. J.: Endogene Magerkeit, in Verhandlungen der Gesellschaft für Verdauungs und Stoffwechselkrankheiten, IX. Tagung in Berlin, 16. bis. 18. Oktober 1929, Leipzig, Georg Thieme, 1930, pp. 96-116.

pituitary signs and subdivided the pituitary form into three groups. His atrophic type would correspond to Simmonds' disease. In his textbook [14] he gave well illustrated descriptions of the various types of pituitary leanness, stressing again the morphologic characteristics of the patients as indicative of the underlying endocrine disorders. Reyé and Schürmann [15] presented a case in which autopsy was performed in 1929 after treatment with "fresh anterior pituitary gland and later with Praephyson" had been administered for eleven years. The autopsy showed complete disappearance of the anterior pituitary. There was no definite evidence of embolism or thrombosis. The authors assumed an "idiopathic" disappearance of the glandular portion of the hypophysis. Venables [16] contributed a clinical paper with vivid descriptions of some cases of anorexia nervosa and with some keen comments on the psychologic problem. Conybeare,[17] under the title "A Fatal Case of Anorexia Nervosa," described a woman of 42 who had been told to fast, then lost her appetite and finally died of an infection. The brain was not examined. Josefson [18] gave the details of a case of cerebral "magersucht" which was strikingly similar to the picture of pituitary cachexia; autopsy revealed a pinealoma and sclerosis of the hypophysis. Grafe [19] in his textbook gave a classification of malnutrition and, discussing the influence of hunger on the oxygen consumption, pointed out that not all patients, even those with the most striking cachexia due to starvation, have a low basal metabolic rate. Steinitz [20] expressed the opinion that pituitary cachexia was not necessarily due to a destruction or disappearance of the anterior lobe but often rather to diminished function in cases with reparable changes. He thought that there was a predisposition to the disease not only in the puerperium but also in adolescence. Calder [21] wrote one of the first papers on the subject in this country under the heading of anterior pituitary insufficiency (Simmonds' disease). He pointed out that "the general slowing of all bodily processes, including general muscular debility, gastrointestinal atony, vasomotor weakness and decrease in the basal metabolic rate, present a striking similarity to the phenomenon of hibernation which long has been considered to be under the control of the pituitary gland." He also gave an abstract of all cases of "anterior pituitary insufficiency" up to 1931 (seventy cases) and emphasized the disturbance of the carbohydrate metabolism in these cases. Striker [22] reported "a case of Simmonds' disease with recovery," a girl of 17 weighing 22 Kg., her basal metabolic rate being —48 per cent. Prominent symptoms were abdominal cramps and addiction to cathartics. Brougher [23] observed a 63 year old man whose pituitary cachexia was considered to be due to a chromophobe adenoma. Antuitrin injections were followed by "very definite improvement." Silver,[24] suggesting the name cachexia hypophyseopriva, said that the disease had been almost completely ignored in the American literature. His patient, a 53 year old woman, had lost 53 per cent of her body weight before she died. Grote and Meng [25] reported two typical examples, asserting that one patient was cured by insulin and the other by psychotherapy. Von Bergmann [26] expressed his disbelief in the so-called primary psychogenic types. He lost one patient with pituitary leanness. The anterior pituitary lobe showed "only slight changes as might be expected in death from starvation." He [27] and Sauerbruch strongly recommended implantation of calf hypophysis into the omentum. Schürmann [28] thought that in his case the histologic picture of the pituitary did not suffice to explain the cachexia. Veil and Sturm [29] found diminution of the blood iodine after hypophysectomy. Weinstein [30] reported that from 30 to 35 per cent of the anterior lobe in his case of pituitary cachexia (due to a tumor) was found to be normal histologically. Rose and Weinstein [31] in another case found atrophy, fibrosis and destruction of the normal architecture in the anterior pituitary, adrenal cortex and thyroid gland. Gunther and Courville,[32] having seen at autopsies partial or complete atrophy of the hypophysis without the clinical picture of Simmonds' disease, concluded that some other factors are partially responsible, such as the time element, the existence of just enough tissue to maintain function, or other factors not well understood. Schüpbach [33] warned against insulin treatment. He saw continued improvement in spite of discontinuation of endocrine therapy. He felt that endocrine therapy induced stimulation of function (funktionsbelebung). Wahlberg [34] observed a patient who first showed symptoms and signs of hyperthyroidism and obesity and later developed those of hypothyroidism and leanness (tachycardia with a rate of 120 changed to bradycardia with 52). All of his three patients had "madonna" fingers. Dunn [35] reported a case of "Simmonds' disease" with recovery, as did Hawkinson,[36] who thought that the syndrome might have been caused by transient functional disorder of the anterior pituitary body as well as by neoplastic involvement. Ryle [37] saw fifty-one cases in his consulting practice, only six in hospital practice. He says "We should not search for a solitary causa causans but rather remain constantly alive to the existence of multiple contributory factors." He saw four deaths, two of the fatal cases having been

14. Thannhauser, S. J.: Lehrbuch des Stoffwechsels und der Stoffwechselkrankheiten, Munich, J. F. Bergmann, 1929.
15. Reye, E., and Schürmann, P.: Ueber Simmonds'sche Krankheit, Klin. Wchnschr. **9:** 525 (March 15) 1930.
16. Venables, G. F.: Anorexia Nervosa: A Study of the Pathogenesis and Treatment of Nine Cases, Guy's Hosp. Rep. **80:** 213 (April) 1930.
17. Conybeare, J. J.: A Fatal Case of Anorexia Nervosa, Guy's Hosp. Rep. **80:** 30 (Jan.) 1930.
18. Josefson, A.: Cerebrale Magersucht, Acta med. scandinav. **75:** 507, 1931.
19. Grafe, E.: Die Krankheiten des Stoffwechsels und ihre Behandlung, Berlin, Julius Springer, 1931.
20. Steinitz, E.: Ueber hypophysäre Kachexie und verwandte Zustände, Deutsche med. Wchnschr. **58:** 1323 (Aug. 19) 1932.
21. Calder, R. M.: Anterior Pituitary Insufficiency (Simmonds' Disease), Bull. Johns Hopkins Hosp. **50:** 87-114 (Feb.) 1932.
22. Striker, Cecil: A Case of Simmonds' Disease (Cachexia Hypophyseopriva) with Recovery, J. A. M. A. **101:** 1994 (Dec. 16) 1933.
23. Brougher, J. C.: Pituitary Cachexia: Report of Patient Treated with Anterior Pituitary Extract, Endocrinology **17:** 128 (March-April) 1933.
24. Silver, Solomon: Simmonds' Disease (Cachexia Hypophyseopriva): Report of Case with Postmortem Observations and Review of Literature, Arch. Int. Med. **51:** 175 (Feb.) 1933.
25. Grote, L. R., and Meng, H.: Ueber interne und psychotherapeutische Behandlung der endogenen Magersucht, Schweiz. med. Wchnschr. **64:** 137 (Feb. 17) 1934.
26. von Bergmann, G.: Magerkeit und Magersucht, Deutsche med. Wchnschr. **60:** 123 (Jan. 26), 159 (Feb. 2) 1934.
27. von Bergmann, G.: Magerkeit und Magersucht, München. med. Wchnschr. **81:** 37 (Jan. 5) 1934.
28. Schürmann, P., in discussion on von Bergmann.[26]
29. Veil, W. H., and Sturm, A.: Die Klinik der Hypophysenkrankheiten, München. med. Wchnschr. **82:** 5 (Jan. 3) 1935.
30. Weinstein, A.: Multiglandular Syndromes Resembling Simmonds' Disease, with Case Report, Am. J. M. Sc. **189:** 245 (Feb.) 1935.
31. Rose, E., and Weinstein, George: Cachexia Hypophyseopriva (Simmonds' Disease) with Thyroid and Suprarenal Insufficiency, Endocrinology **20:** 149 (March) 1936.
32. Gunther, L., and Courville, C. B.: Hypophysial Cachexia (Simmonds' Disease) with Atrophy of the Anterior Lobe of the Pituitary Gland, J. Nerv. & Ment. Dis. **82:** 40 (July) 1935.
33. Schüpbach, A.: Zur Hormonbehandlung der Simmonds'schen Krankheit und verwandter asthenischer Zustände, Schweiz. med. Wchnschr. **66:** 1245 (Dec. 12) 1936.
34. Wahlberg, J.: Hypophyseothyrogenic Adiposity and Emaciation, J. A. M. A. **106:** 1968 (June 6) 1936.
35. Dunn, C. W.: Report of a Case of "Simmonds' Disease," with Recovery, J. Nerv. & Ment. Dis. **83:** 166 (Feb.) 1936.
36. Hawkinson, L. F.: Simmonds' Disease (Pituitary Cachexia): Report of Case in Which Patient Responded to Anterior Pituitary-like Principle of Pregnancy Urine, J. A. M. A. **105:** 20 (July 6) 1935.
37. Ryle, J. A.: Anorexia Nervosa, Lancet **2:** 893 (Oct. 17) 1936.

labeled psychotic, ". . . and yet some of the psychoneurotics who did well might, I surmise, under adverse circumstances, have drifted as badly." He thought that the reappearance of menstruation was the best criterion of cure. Krause [38] expressed the belief that the cachexia of the pituitary insufficiency is due to shrinkage of the adrenal cortex. Seemingly miraculous return of appetite followed injections of adrenal cortex extract. Gallavan and Steegmann [39] reported two cases of "Simmonds' disease" with autopsy. Kylin [40] described fourteen cases in detail with two autopsies. He thinks that the syndrome is the opposite of Cushing's syndrome. He is enthusiastic about implantation of calf hypophysis. Recently in a paper with many photomicrographs Sheehan [41] expressed the opinion that necrosis of the anterior pituitary is relatively frequent in women dying during the puerperium. The necrosis, beginning about the time of delivery, is due to thrombosis of pituitary vessels, not to embolism. Sheehan and Murdock [42] state that "in patients who have a postpartum necrosis of the anterior pituitary a subsequent pregnancy is possible if genital atrophy has not taken place. Such a pregnancy usually brings great improvement or even complete and permanent cure of the symptoms of pituitary insufficiency." Von Weizsäcker,[43] in reporting two well studied cases, stresses the psychologic element. Straube [44] discusses the treatment. Kunstadter [45] strangely calls the syndrome "von Bergmann's disease." Stroebe [46] (von Bergmann's clinic) gives two interesting autopsy reports of cases with late adolescence cachexia and similar postmortem observations. There were no gross anatomic changes in the hypophysis and no necrosis of the anterior lobe as described by Simmonds. He points to the history of the cases as showing an overwhelmingly negative attitude toward life in the beginning of the emaciation. Herrick,[47] in a recent monograph on the pituitary gland, gives only a brief discussion of the problem. He assumes that Falta's so-called pluriglandular sclerosis is nothing more than pituitary cachexia. The pendulum seems to swing back from overemphasis on the endocrine etiology in a paper by Farquharson and Hyland.[48] Richardson [49] reported six cases, one of them fatal, autopsy revealing no essential changes in the pituitary gland; he concluded that Simmonds' disease, in the sense of a destructive lesion of the pituitary body, is rare and anorexia nervosa with the signs of Simmonds' disease much more common.

Within the last year a number of papers on the subject have appeared, a few of which may be mentioned. Sheldon and Young [50] studied the carbohydrate metabolism in cases of anorexia nervosa. Bruckner, Wies and Lavietes [51] state that a satisfactory means of differentiating Simmonds' disease from anorexia nervosa has not yet been established. Morlock [52] gives details of a young man with the syndrome (it is encountered rarely in the male sex). Plummer and Jaeger [53] also describe a male patient with many features of Simmonds' syndrome, complicated, however, by polyuria, optic atrophy and other features due to a glioblastoma multiforme involving the tuber cinereum and adjacent structures. Rahman, Richardson and Ripley [54] give details of their psychiatric studies in twelve cases.

This review of part of the important literature on the subject makes no endeavor to be complete, leaving out purposely all experimental work as being beyond the scope of this clinical report.

The following three cases were observed at the Diagnostic Hospital within the last few years:

REPORT OF CASES

CASE 1.—P. T., a girl aged 14 years, American of Italian stock, admitted June 12, 1933, because of loss of weight, was referred by Dr. A. F. Bronner and Dr. William Healy of the Judge Baker Child Guidance Center. She stated that in December 1931 she had been told by the school physician that she was overweight. According to the school record she then weighed 120 pounds (54 Kg.), while the average weight for her height would have been 95 pounds (43 Kg.). The mother, however, claimed that she never looked fat but "just right." The girl tried to lose weight by reducing her food intake. Having done so for some time with difficulty, she then in March 1932 lost her appetite completely. When forcing herself to eat, she felt abdominal distress and vomited several times. Whereas she had previously been an active girl, she became lazy and complained of feeling tired. Her weight finally dropped to 72 pounds (33 Kg.), a loss of almost 50 pounds (23 Kg.). She was sent to a sanatorium, where forced feeding for four months resulted in a gain of only 2½ pounds (1 Kg.), which she promptly lost after returning home. She suffered from constipation. Her periods, beginning at the age of 11 years, had been regular for two years until August 1932, when they ceased. Her past and family histories were noncontributory. Her mother appeared high strung. Closer questioning revealed marked antagonism of the girl toward her family and strong emotional conflicts. She felt particularly unhappy at home after her grandmother, to whom she had been very much attached, had left the family in April 1933.

On admission she was extremely undernourished, weighing 76½ pounds (35 Kg.) and measuring 5 feet ¼ inch (153 cm.) in height. Her skin was dark, but this was thought to be a racial characteristic. It was covered with fine fuzzy lanugo hair, particularly on the back and neck but also noticeable on the arms and legs (fig. 1). The skin appeared dry and slightly scaly over the abdomen. There was a normal amount of hair on the scalp; there were thick eyebrows and a distinct mustache; the teeth were fair. The fundi and visual fields were normal; the thyroid gland was not enlarged. The lungs were normal to percussion and auscultation; the heart showed a small absolute and relative dulness. The resting heart rate was 34 per minute; there was a quick rise to over 100, however, even with slight exercise. The electrocardiogram showed no abnormalities except the extreme sinus bradycardia. The blood pressure was 80 mm. of mercury systolic, 60 mm. diastolic. The

38. Krause, F.: Die Erkrankungen des Hypophysenvorderlappens, Klinische Fortbildung, Berlin, Urban & Schwarzenberg, 1937.

39. Gallavan, M., and Steegmann, A. T.: Simmonds' Disease (Anterior Hypophysial Insufficiency): Report of Two Cases with Autopsy, Arch. Int. Med. **59**: 865 (May) 1937.

40. Kylin, E.: Magersucht in der weiblichen Spätpubertät. Ein eigentümliches Krankheitsbild sui generis, Deutsch. Arch. f. klin. Med. **180**: 115, 1937.

41. Sheehan, H. L.: Postpartum Necrosis of the Anterior Pituitary, J. Path. & Bact. **45**: 188 (July) 1937.

42. Sheehan, H. L., and Murdock, R.: Postpartum Necrosis of the Anterior Pituitary: Effect of Subsequent Pregnancy, Lancet **2**: 132 (July 16) 1938.

43. von Weizsäcker, V.: Ueber Träume bei sogenannter endogener Magersucht, Deutsche med. Wchnschr. **63**: 253 (Feb. 12) 1937.

44. Straube, G.: Zur Therapie der Simmonds'schen Krankheit, Klin. Wchnschr. **17**: 1016 (July 16) 1938.

45. Kunstadter, R. H.: Pituitary Emaciation (von Bergmann), Endocrinology **22**: 605 (May) 1938.

46. Stroebe, F.: Zum Problem der endogenen Magersucht; abstracted, Zentralbl. f. inn. Med. **59**: 97 (Feb. 5) 1938.

47. Herrick, W. W.: The Pituitary Gland, Baltimore, Williams & Wilkins Company, 1938, p. 609.

48. Farquharson, R. F., and Hyland, H. H.: Anorexia Nervosa: A Metabolic Disorder of Psychologic Origin, J. A. M. A. **111**: 1085 (Sept. 17) 1938.

49. Richardson, H. B.: Simmonds' Disease and Anorexia Nervosa, Arch. Int. Med. **63**: 1 (Jan.) 1939.

50. Sheldon, J. H.: Anorexia Nervosa with Special Reference to Physical Constitution, Lancet **1**: 369 (Feb.) 1937. Sheldon, J. H., and Young, F.: On the Carbohydrate Metabolism in Anorexia Nervosa, ibid. **1**: 257 (Jan. 29) 1938.

51. Bruckner, W. J.; Wies, C. H., and Lavietes, P. H.: Anorexia Nervosa and Pituitary Cachexia, Am. J. M. Sc. **196**: 663 (Nov.) 1938.

52. Morlock, C. G.: Anorexia Nervosa, Proc. Staff Meet., Mayo Clin. **14**: 24 (Jan. 11) 1939.

53. Plummer, D. E., and Jaeger, J. R.: Pituitary Cachexia (Simmonds' Disease): Report of a Case with Autopsy, Arch. Neurol. & Psychiat. **40**: 1013 (Nov.) 1938.

54. Rahman, L.; Richardson, H. B., and Ripley, H. S.: Anorexia Nervosa with Psychiatric Observations, Psychosom. Med. **1**: 335 (July) 1939.

abdomen showed a scaphoid contour. The clitoris was not remarkable; the uterus on rectal examination was thought to be about one third normal size. The extremities appeared disproportionately long, but the relation of standing to sitting height was 1.9 to 1.0.

The patient's psyche was peculiar, depressed, even sullen and brooding at times; she seemed bright and willing to cooperate, however. The mouth temperature was subnormal, being

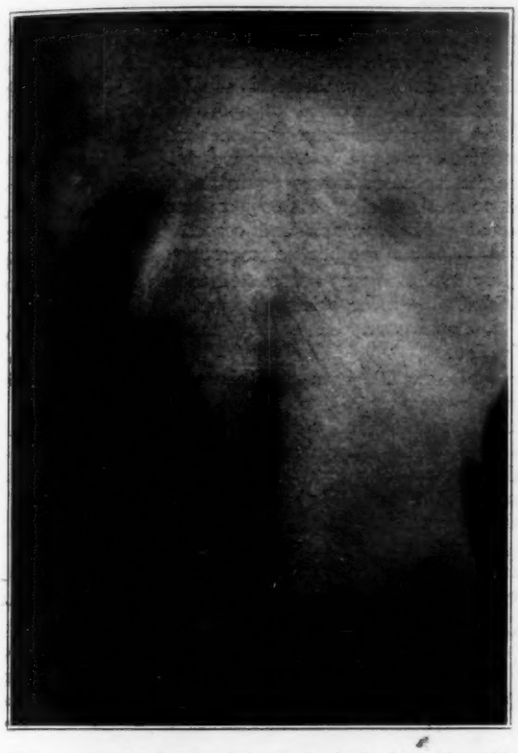

Fig. 1 (case 1).—Lanugo hair on the back, June 29, 1933.

as low as 95 F. and usually around 97. On June 16 the twenty-four hour urine specimen measured 380 cc., with a specific gravity of 1.012. On June 17 the figures were 270 cc. and 1.017. There was no albumin or sugar or other abnormality in the urine. During the first four hours following the ingestion of 1,500 cc. of water for a dilution and concentration test of kidney function there was an output of only 275 cc. instead of the usual 1,300 to 1,700 cc. This was due not to absolute fluid retention but to a delay in excretion, for in the next four hours the output had increased to 715 cc. instead of decreasing as usual. The maximum dilution was to 1.001 in three hours after ingestion of 1,500 cc. of water and the concentration to 1.017 in thirty hours after the ingestion of this fluid, during which time she received no fluids. A striking feature was the girl's indifference to this thirsting experiment, which was carried out on a hot summer day. When everybody else was perspiring and thirsty, she didn't seem to mind the heat and was by no means anxious to drink water even at the end of the experiment. A complete blood count, blood sedimentation rate and Hinton, Wassermann and Kahn tests were normal. The fasting blood sugar was 80 mg. per hundred cubic centimeters. On another day, after a fasting blood sugar of 92 mg. per hundred cubic centimeters, 100 Gm. of dextrose was given orally. The values were as follows: after one half hour 96 mg., after one hour 110 mg., after two hours 137 mg. and after three hours 162 mg. per hundred cubic centimeters. The urine specimens taken at the same time showed no sugar. Frequent basal metabolic rate determinations varied between —42 and —22 per cent. Determination of the specific dynamic action of 200 Gm. (uncooked weight) of beefsteak, attempted with the standard Benedict machine, showed an increase of only 27 calories over the initial level within five hours. X-ray examination of the skull showed a sella turcica of normal contours; the lung fields were clear.

An attempt was made to force food, but this proved unsatisfactory since the patient would eat only small amounts. Daily injections of 1 cc. of antuitrin were given for two weeks, also antophysin and later theelin, without results. Then Armour's thyroid was given, 1½ grains (0.1 Gm.) for one day, 1½ grains twice a day for one day and 1½ grains three times a day for five days. Following this thyroid therapy her resting pulse rate, which regularly had been between 34 and 50 per minute, rose to about 70 and her basal metabolic rate rose to —22 per cent. Her appetite, however, was not improved and her weight dropped to 69 pounds (31 Kg.) from 74½ pounds (34 Kg.). After she had been observed for forty-eight days with no improvement except a persistent elevation of pulse and temperature after thyroid therapy she was given insulin, beginning with 2 units twice daily, increasing to 8 units twice daily, combined with 100 Gm. of dextrose added to breakfast and the midday meal when she received the injections. She began to gain a few pounds but had a mild insulin reaction with a blood sugar of 57 mg. per hundred cubic centimeters three hours after an injection. She was then kept in bed, insulin therapy was cautiously continued, and 100 Gm. of lactose was added to the 200 Gm. of dextrose. Her face began to look slightly puffy. During thirty days of insulin treatment her weight increased from 70 to 83 pounds (32 to 38 Kg.). She stated that her appetite had improved, but she continued to be restless and it was difficult to keep her in bed. At this time a dilution and concentration test showed normal excretion of water (805 cc. within four hours after the ingestion of 1,000 cc. of water), a dilution of the urine to 1.001 after three hours and a concentration to 1.026 when fluids had been withheld for twenty-two hours. The twenty-four hour urine amount was now about 2,000 cc. with a specific gravity of 1.010. The blood pressure was 92/70 at this time. There was still no menstruation. She seemed so nearly normal at this time, however, that insulin was omitted, the dextrose feedings and the diet remaining unchanged. In the next forty days her weight rose from 83 to 95 pounds (38 to 43 Kg.). During the following twenty-two days, when insulin again was added, her weight rose to 102 pounds (46 Kg.), the increase now being no more rapid than without insulin. The basal metabolic rate at this time was —26 per cent. A dextrose tolerance test was normal, the fasting blood sugar being 92 mg. per hundred cubic centimeters. One half hour after 100 Gm. of dextrose was given orally it was 193 mg., one hour later 145 mg., two hours later 119 mg. and three hours later 96 mg. Because the basal metabolic rate was still low, thyroid 1 grain (0.06 Gm.) three times daily was again given, this time for eight days. The basal metabolic rate rose to —16 per cent but there was also a loss in weight from 102 to 98½ pounds (46.3 to 44.7 Kg.), so the thyroid was discontinued. In the next week she regained the 3½ pounds and was discharged home improved but apparently not cured, with a total gain in weight of about 30 pounds (14 Kg.).

Fig. 2 (case 1).—Appearance of patient during July 1934; weight 73½ pounds.

The following note on her emotional state before, during and after her hospital stay was made by Dr. A. Bronner: "Before she went to the hospital she was irritable, but mildly so, and in

general made very extreme overstatements of the goodness of her parents, especially her mother, and of their many sacrifices. She showed some stubbornness in holding on to her own ideas. As she came to see me toward the end of her hospital stay she seemed cheerful, happy and amenable, expressed gratitude for all that was being done and continued her kindly attitude

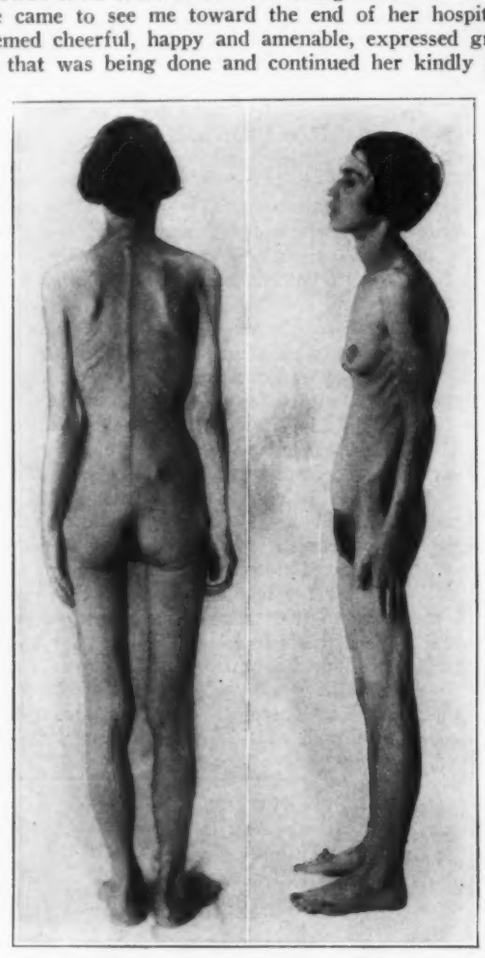

Fig. 3 (case 1).—Rear and side views during July 1934.

toward her parents. Since she has returned home there has been a marked change. In her home and here in her interviews she has revealed earlier hidden deep antagonisms toward her parents, of whom she is now very critical. She seems markedly antagonistic, unhappy and very stubborn and discontented. The psychiatric study and treatment of her deep-seated emotions that probably underlie her eating problem are in the very early stages."

The second admission to the Diagnostic Hospital took place July 6, 1934, because she had soon lost appetite and weight at home and had complained of epigastric pain and of a cough, three months previously, which had lasted for a month.

She was now 15 years old; her weight had dropped to 73½ pounds (33 Kg.). Her general appearance is noted in figures 2 and 3. She looked very much as she had in 1933 at the first admission. Her basal metabolic rate varied between —25 and —30 per cent; the pulse rate and temperature were higher than one year before. Insulin and diet therapy did not bring about a gain of more than 3½ pounds (1.5 Kg.) in five weeks. She hid and discarded food and appeared introspective. She appeared to enjoy the experience of being an interesting case. On August 10 she was given 10 Gm. of sodium chloride in capsules, and the dose was given daily thereafter for three weeks. Her temperature rose to 101 F. the evening of August 10 and continued between 100 and 103 F. for two weeks. X-ray examination of the lungs showed consolidation and a small cavity in the right upper lobe. The sputum was positive for tubercle bacilli. A most interesting feature of the further course was the fact that she gained about 8 pounds (3.6 Kg.) during the febrile stage and continued to gain weight while arrangements were being made to transfer her to a tuberculosis sanatorium. When she left for the North Reading Sanatorium on October 11, with the diagnosis of open active bilateral pulmonary tuberculosis, her weight was 110 pounds (50 Kg.); she had gained over 35 pounds (16 Kg.) during the two months when she was febrile. Her basal metabolic rate was between —2 and —7 per cent during the febrile state, the hemoglobin had dropped to 67 per cent (72 per cent in July 1934), the dextrose tolerance curve was normal, but the blood sedimentation rate and the white count were distinctly elevated. Figure 4 shows the patient before she was transferred to the sanatorium, where she was treated for almost four years. After an attempt to collapse the right lung was unsuccessful, pneumothorax on the left and, in 1936, pneumolysis were done. During the treatment her weight increased to approximately 135 pounds (62 Kg.), but after the pneumolysis she had temporary recurrence of fever and cough and lost some weight. During 1937 and 1938 her weight increased slowly again and the tuberculous process tended to heal, finally reaching an apparently arrested state. Menstrual periods, which had ceased in 1932, had returned twice in 1935, but she has not menstruated since.

In July 1938 she was readmitted to the Diagnostic Hospital for a third time to be briefly observed. She continued to complain of impaired appetite, easy fatigability, poor sleep and constipation.

She was now 19 years old; she was still definitely undernourished, weighing 98¾ pounds (45 Kg.), and her height was 5 feet 1½ inches (156 cm.), an increase of only 1¼ inches since 1933. The fuzzy lanugo hair was still prominent; the skin, however, was not dry and she seemed to perspire normally. The lungs showed evidence of healed tuberculosis of the right upper lobe and pneumothorax on the left side. The heart was normal, the pulse rate 67; on admission her blood pressure was 92/56 and later 120/80. Gynecologic examination showed the uterus to be infantile. The temperature was normal.

Fig. 4 (case 1).—Improvement shown in October 1934; weight 110 pounds.

The blood picture was essentially normal but the blood sedimentation rate was still elevated, 38 mm. in sixty minutes (Westergren). The dextrose tolerance curve was within normal limits, the basal metabolic rate —13 per cent; the daily urinary nitrogen excretion ranged between 3.5 and 5 Gm., and the sodium chloride excretion was also low.

She was discharged home to have regular pneumothorax refillings ambulatorily and maintained her weight until December 1938, when there developed pitting edema of both legs and puffiness of the face. During the fall of 1938, when a root canal had been filled in one tooth, this tooth had suddenly broken in half.

On her fourth admission to the hospital, Feb. 24, 1939, the patient weighed 103½ pounds (47 Kg.), the increase in weight being obviously due to rather marked edema. About a month later, with the disappearance of the edema, her weight had dropped to 85.8 pounds (39 Kg.). On discharge, March 2, her weight had reached 98 pounds (44.5 Kg.) again. Except for the edema and a split premolar tooth, physical examination revealed no new abnormalities. The pulse rate was 48 per minute, the blood pressure 108/70. The pneumothorax was fairly complete, with only a small amount of effusion in the left side of the chest, the pulmonary tuberculosis being apparently arrested, as indicated by the x-ray examination, normal temperature, a normal blood sedimentation rate and the absence of tubercle bacilli in the scanty sputum. Of interest were the reduced serum albumin values, the figures being as follows: On Feb. 27, 1938, the total serum protein was 4.01 Gm., the serum albumin 1.84 Gm. and the serum globulin 2.17 Gm. per hundred cubic centimeters. After much coaxing and admonition she ate somewhat better during the stay in the hospital, although we were unable ever to make her eat a full meal and, in view of our previous experience with this type of patient, could never be sure of how much of the food on the tray she had actually consumed and how much had disappeared in some other way. However, the serum protein readings increased as the edema diminished, the total protein being 5.35 Gm., the albumin 3.38 Gm. and the globulin 1.97 Gm. on March 14, 1939. A dextrose tolerance curve was within normal limits; the basal metabolic rate was —31 per cent.

Efforts at psychotherapy and the plan to have the girl go to a foster home in order to eliminate the environmental influences of her home have not succeeded very well as yet, mostly on account of the lack of cooperation on the part of her domineering, rather unintelligent, very robust mother. After discharge from the hospital she was followed as an ambulatory patient, her condition remaining essentially unchanged. The pulmonary process continues arrested, the edema is returning slightly, and the amenorrhea continues.

CASE 2.—R. J., a girl aged 14 years, American, also referred by Dr. A. F. Bronner and Dr. William Healy from the Judge Baker Child Guidance Center in November 1933, stated that she had been well until she had scarlet fever at the age of 9. During the time of recovery she had a very good appetite and put on much weight. Two years later she weighed 126 pounds (57 Kg.) and children, as well as teachers and relatives, began to tease her because she was "too fat." With the help of an insurance pamphlet she put herself on a diet in March 1933, selecting 1,400 calories from the given samples. In the six months of self-inflicted diet she lost at least 40 pounds (18 Kg.). Admitting that she was now too thin, she said she was afraid to eat since she might then gain too much weight and everybody would tease her again. She was ambitious in school and much concerned about her marks. She did not complain of abdominal pain except during her periods, which, however, had ceased in February 1933, after having been somewhat irregular following the menarche at the age of 12. Because of habitual constipation she had taken laxatives of various descriptions.

The family history was not contributory except for a tendency to leanness in the girl's family. Her parents were slender; her paternal grandmother had never weighed more than 95 pounds (43 Kg.) until her menopause.

Examination showed that she was emaciated. She weighed 80 pounds (36 Kg.). Her height was 5 feet 2¼ inches (158 cm.). All ribs could easily be seen; the skin over the crista ilii was stretched and irritated and appeared slightly dry and scaly. Her hands and feet were cool but not cyanotic. Her face was that of an old woman (fig. 5), with sunken cheeks and with wrinkles. The hair of the scalp was dry, short and thin, the eyebrows normal and the pubic and axillary hair scanty. The teeth were in good condition. The fundi and visual fields were normal and the thyroid not enlarged. The lungs and heart were normal to percussion and auscultation and also on x-ray examination. The pulse rate was 44 per minute in the recumbent [the electrocardiogram showed sinus bradycardia] and 80 per minute in the erect position. The blood pressure ranged between 75/60 and 85/60. The abdomen was scaphoid.

The patient was intelligent, at times depressed, rarely smiling and occasionally antagonistic and morose. According to Dr. Anna M. Skinner, when first seen she was distinctly disturbed emotionally, very antagonistic toward her parents, gave many evidences of a strong feeling of guilt, threatened suicide and seemed depressed.

Fig. 5 (case 2).—Appearance of patient in November 1933; weight 80 pounds.

Her temperature was at times slightly subfebrile. Laboratory studies showed a normal urine, blood picture and serologic reaction. The twenty-four hour urine amount once was as low as 220 cc. with a specific gravity of 1.038. The dilution and concentration tests showed a delayed water output (730 cc. only four hours after the ingestion of 1,000 cc. of water). The blood sedimentation rate was 1 mm. in sixty minutes. The fasting blood sugar value was 73 mg.; one-half hour after administration of 100 Gm. of dextrose 103 mg., one hour later 109 mg., two hours later 105 mg. and three hours later 95 mg. per hundred cubic centimeters. The basal metabolic rate on admission was —31 per cent; three weeks later it was —49 per cent.

The patient was given a high caloric diet, which however most of the time she did not eat. Two cc. of antophysin was injected daily for one week without demonstrable effect. After eleven days in the hospital she had gained only 1 pound (0.5 Kg.). Insulin in small doses, from 2 to 8 units twice daily combined with 100 Gm. of dextrose in orange juice, was then given daily. From this time on she decidedly began to gain weight. In a few weeks there took place gradually a complete change in her personality. She would not remain in bed as

advised, had no complaints and was eager to help in the treatment and stated that she felt like an entirely different person. In thirty-eight days her weight increased from 81 to 100 pounds (37 to 45 Kg.) and she was discharged, apparently normal in every respect except for the persistent amenorrhea (fig. 6). Her basal metabolic rate was now —2 per cent; the blood pressure had risen to 100/68; the fasting blood sugar was 90 mg. per hundred cubic centimeters. A dextrose tolerance test now showed a rise to 137 mg. in one hour and a return to 95 mg. in three hours. The twenty-four hour urine was now between 800 and 1,200 cc. with the specific gravity ranging between 1.011 and 1.016.

Dr. Skinner wrote that the first two weeks after leaving the hospital, when placed in a foster home, the patient was again greatly upset though not as much as originally. She

Fig. 6 (case 2).—Improvement shown by January 1934; weight 100 pounds.

was irritable and resentful of criticism. Now, with continued psychiatric help and the management of an apparently very good foster mother, she seems more stable.

She remained well, was menstruating regularly when seen in 1938 and looked and acted like a perfectly normal, well composed young lady.

She was readmitted on Oct. 27, 1939. At this time we learned that she had had no menses for twelve months, the periods having been normal for four years previously. In January 1939, for no apparent reason, edema began to develop. This was recurrent and progressive until the time of her last admission. Her weight, which had been about 118 pounds (54 Kg.) for several years, decreased to 105 pounds (48 Kg.) in September and October 1938, when she was having emotional difficulties with her "boy friend." The amenorrhea began during this period and might be attributed either to the relatively slight weight loss or to the emotional trauma. The edema was not satisfactorily explained after full investigation in the hospital.

Obviously some abnormality persists. We can only conclude that it is safer to designate improved cases of anorexia nervosa as temporarily recovered rather than cured.

CASE 3.—M. H., a woman aged 28, of English stock, a housewife, was admitted twice within a relatively short time in 1935 and 1936. The case history may be summarized as follows:

Symptoms began about one year after her marriage at the age of 20. She had then continued to work in a mill, getting up before 6 o'clock in the morning, doing the housework, working all day in the mill, and working again at home until midnight. She said that she became extremely nervous and irritable and that her stomach began to feel heavy after eating. Soon she vomited after every meal food which was not digested at all. She felt that her "stomach got worked up" whenever she became excited. There were times, she said, when she felt as if the inside of her stomach was tied up in a knot. After having vomited after practically every meal for years she then, at the age of 26, began to vomit blood. From then on she had vomited blood about seventy times. According to her statements the amount of blood varied from a teaspoon to a cup. The hematemesis occurred only after a large meal and she felt relieved afterward. From this time on she lost weight rapidly, although there had been a gradual loss from 126 pounds (57 Kg.) at the time she was married to 111 pounds (50 Kg.) when she began to vomit blood. From 111 pounds her weight fell to 75 pounds (34 Kg.) in 1935, at which time she was admitted to the hospital. However, she claimed that her appetite was good and that she could always eat. The vomiting of blood had been less frequent during the last year, but she continued to vomit at least once a day. She had suffered from constipation for many years. She dreaded cold weather; her hands and feet would always be cold no matter how heavily she dressed. She had felt dizzy at times outdoors because of the cold and had fainted a few times on such occasions. Her sleep had been very much impaired in the year after marriage, when she continued to work in the mill. She could not stay in bed but would find something to do and "then work, work, work." Even during the more recent years, after she had given up the mill work, she would always drive herself. She asserted that she was never tired and that she was able to stay up until 2 or 3 o'clock in the morning and yet rise very early. She stated that she had many friends, being very popular. Although she said that her marital life was very happy, close inquiry revealed that she had never had sexual intercourse with her husband. She explained this by stating that she had no sexual desire, her husband abstaining when she made that clear. Menstruation had begun at the age of 14 and had been regular until one year after marriage, when the periods ceased permanently.

The past history otherwise was not remarkable. At the age of 9 she had received a prize at a fair for being the healthiest child. One sister had had a nervous breakdown.

Physical examination (fig. 7) showed an extremely undernourished woman, weighing 73 pounds (33 Kg.), who was surprisingly active for her dreadful appearance. She was 5 feet one-fourth inch (153 cm.) tall. The skin was thin, translucent and parchment-like where it was stretched over the bony ridges. The abdomen showed definite striae, obviously due to the tension of the tightly stretched skin. There was slight brown pigmentation over the sacral and anal regions and also over the shins and crista ilii. The skin was dry; the underlying muscles could be seen as through a movable veil. No spontaneous petechiae were seen, but the tourniquet test was slightly positive. The hair and eyebrows were abundant. The teeth were in fair condition. The heart and lungs were normal to percussion and auscultation. The pulse rate was between 50 and 60 and once 48 per minute. The blood pressure was 84/62. The abdomen was scaphoid; the lower pole of the right kidney was easily palpable. Gynecologic examination was difficult on account of the patient's lack of cooperation. It disclosed a tight hymenal ring admitting one finger with difficulty.

Personality studies, already partially given in the history, showed an extremely nervous temperament, excitability, stubbornness and fussiness. The patient seemed driven by an inner impulse which never gave her any rest, rendering her unable to relax.

Her temperature was subnormal, several times being 96 F. Laboratory studies revealed a normal blood count with the exception of a diminished platelet count, which varied between 170,000 and 280,000 per cubic millimeter. The blood sedimentation rate and Hinton, Wassermann and Kahn tests were normal. Bleeding and clotting time were within normal limits. The fasting blood sugar was 79 mg. per hundred cubic centimeters. The serum cholesterol was 163 mg. per hundred cubic centimeters with a normal ratio between esters and free cholesterol. The urine contained no pathologic substances. The dilution and concentration test showed a markedly delayed water output (320 cc. only four hours after the ingestion of 1,000 cc. of water) with the lowest specific gravity 1.006, the highest being 1.028. The twenty-four hour urine volume was low (the smallest amount measuring 186 cc.) with a correspondingly low twenty-four hour urinary nitrogen excretion of only 1.86 Gm. on one day and frequently between 2 and 3 Gm. on other days. The basal metabolic rate was repeatedly about —20 per cent and once —29 per cent. The electrocardiogram was normal; the x-ray examination of the esophagus and stomach revealed no evidence of pathologic changes. X-ray study of the chest showed spontaneous fractures of three ribs, which on reexamination one year later had healed. The skeleton showed a diminished calcium content throughout, which was particularly obvious in the skull. There was also callus formation in the inferior ramus of the right pubic bone. Dr. G. W. Holmes thought that the bones were somewhat decalcified and commented that a high degree of decalcification on animal experiment leads to spontaneous fractures. It was thought that the fractures may have occurred from falls associated with the fainting spells.

Dr. J. J. Schloss performed a gastroscopy and found multiple pinpoint hemorrhages which he thought were due to the frequent vomiting spells. Gastric analysis revealed no free hydrochloric acid after a caffeine meal.

Attempts at psychotherapy proved unsuccessful. The frequent vomiting prevented adequate high caloric and vitamin intake of food. The vomitus contained only traces of blood while the patient was in the hospital. Her weight varied between 74 and 64 pounds (34 and 29 Kg.). She insisted on going home, her condition being essentially unchanged.

Fig. 7 (case 3).—Appearance of patient in November 1936; weight 73 pounds.

Rather unexpectedly we saw the patient again in November 1938. Her appearance had changed markedly; she had gained about 20 pounds (9 Kg.) in the last two years, weighing now 92½ pounds (42 Kg.). She stated that after leaving the hospital she began to eat small meals and that it seemed necessary to humor the stomach and let it stretch gradually over a period of a year. In 1937, however, she began to eat regularly and had since been able to do this with comfort, boasting of being able even to eat doughnuts and pork chops. She did not vomit again. She now slept well and felt much more restful. There were no menstrual periods yet, however, and she had still had no sexual intercourse with her husband. She admitted having been frightened by the picture which we had made of her at the hospital and said that she couldn't believe that she could look so terrible. She stated that she felt that her extreme emaciation had been due to the fact that in her work she was excessively fatigued and that, in addition to this, her marriage had added housework so that she came to a state in which she could not sleep. She had noticed lately that her hair began to grow normally again, that her skin was warm and that she was not continually "freezing to death" any more.

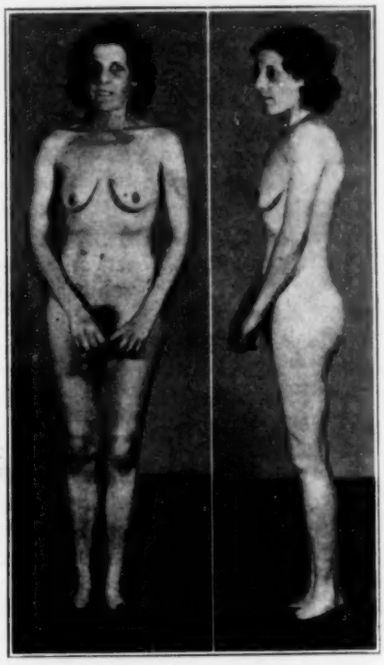

Fig. 8 (case 3).—Improvement by November 1938; weight 92½ pounds.

On physical examination she weighed 92½ pounds and was still spare and lean but very different in appearance from her former state, her skin having lost the parchment-like character (fig. 8). About the edge of her hair there was a short new growth of hair. The eyes, including ophthalmoscopic examination, were normal. The teeth were in good condition. The pulse rate varied between 60 and 70 per minute; the blood pressure was 100/70. Gynecologic examination demonstrated an intact hymen and an extremely small uterine fundus. She was comfortable and cheerful throughout her five day stay in the hospital and gained 1 pound more. Her temperature varied between 97 and 98.4 F. Laboratory studies showed a normal urinalysis, a mild hypochromic anemia, a reduced platelet count of 130,000 per cubic millimeter, and a slightly positive tourniquet test; the fasting blood sugar was 101 mg. per hundred cubic centimeters. After the ingestion of 100 Gm. of dextrose the blood sugar level was 205 mg. after one-half hour, 228 mg. after one hour, 183 mg. after two hours and 127 mg. after three hours. There was a slight spilling of sugar in the urine in the first and second hours of this test. The basal metabolic rate was still —23 per cent. Gastric analysis showed no free hydrochloric acid and a total acidity of 30 degrees. Dr. Schloss repeated the gastroscopy and found the mucosa of the stomach normal with possibly a slight degree of atrophy. An x-ray film of the chest revealed that the previously reported fracture of the ribs had completely healed.

Briefly then there had occurred in this woman a striking change of bodily appearance associated with a change of her personality. She now appeared to be well on her way to recovery although the persistent amenorrhea, as well as the low basal metabolic rate and slight anemia, would make one hesitate to call the recovery complete. It appears that in these cases normal menstruation is the last hurdle to full health.

COMMENT

The recent appearance of many papers dealing with cases similar to those just reported indicates that this syndrome is relatively frequently encountered. These papers have stimulated controversial discussion, particularly as to cause and management.

The problem begins immediately when one tries to label these cases. Those who would like to refer to them as examples of neurosis or anorexia nervosa must explain the striking features which point so decidedly

to an endocrine disturbance. Why are many of the characteristic traits, suggesting hypofunction of various endocrine glands, so similar to the classic signs of Simmonds' disease, or pituitary cachexia, which is generally agreed to be due to atrophy of the anterior pituitary lobe? Emaciation, anorexia, dry cold skin, subnormal temperature, low oxygen consumption, amenorrhea, hypoglycemia, bradycardia, arterial hypotension, low level of water metabolism, constipation and psychic alterations are common manifestations of both anorexia nervosa and pituitary cachexia. Admitting that in cases of "true" fatal Simmonds' cachexia the changes are extreme, one wonders whether the differences are quantitative rather than qualitative. It seems difficult to assume that the loss of hair and teeth and the extreme weakness in pituitary cachexia in contrast to the frequently observed growth of peculiar lanugo-like hair and the psychic alertness and restlessness in anorexia nervosa should signify a totally different etiology. Is it possible that the duration of the illness and the age of the persons involved could account for the difference of the two clinical pictures? Why is true pituitary cachexia always fatal? How is one to recognize mild cases of pituitary cachexia and how is one to differentiate them clinically from instances of anorexia nervosa? Through what mechanism could starvation induce those endocrine features common to the two diseases—through pituitary hypofunction? One might say teleologically that hunger leads to a vita minima. The result of the dilution test in all three cases and the flat, slowly rising dextrose tolerance curve in cases 1 and 2 suggest a delay in handling water and dextrose consistent with the conception of a life on a lower level of activity. The amenorrhea would fit into this idea of a throttled life, like war or starvation amenorrhea (von Noorden and Salomon [55]). Benedict's [56] important work on students who were put on a reduced caloric intake and then showed many of the features which our patients showed, notably lowered oxygen consumption, bradycardia, hypotension and loss of libido and energy, is interesting in this respect, as is the current assumption that the pituitary gland controls hibernation (Calder [21]).

Those, on the contrary, who would be inclined to assume a primary functional endocrine deficiency in order to explain our cases, as has been the tendency lately under the influence of modern experimental and clinical endocrinology, would have to account for the striking psychic abnormalities. With the solution or alleviation of these personality problems and readjustment to life's difficulties, the appetite of most of these patients returns and the endocrine features vanish—a fact that leaves doubt as to their primary nature. This has happened to moribund patients, who might have died had not a physican turned the tide (Venables,[16] Ryle [57]). Should one resort to the term "functional" Simmonds' disease—a pituitary "black out" of psychologic origin, as Sheldon [50] does?

The time relation between pituitary cachexia and the puerperium is striking and can be explained by starvation with difficulty unless we assume that it is during the puerperium when emotional strains most commonly occur. (Approximately 80 per cent of the insanity of pregnancy occurs in the puerperium.) The work of Sheehan,[57] already referred to, appears to be particularly important in this regard. Sheehan and Murdock's statement that a second pregnancy "usually brings great improvement or even complete and permanent cure of the symptoms of pituitary insufficiency" is particularly startling and worthy of further studies. Undisputed appears to be the pathogenesis of the cases with pituitary cachexia due to tumor or granulomatous tissue destroying the anterior lobe. In the reports of embolic or thrombotic phenomena after pregnancy with resulting pituitary atrophy, no adequate explanation of the specific localization of such vascular lesions has been forthcoming. Schürmann [28] reported a complete absence of the anterior lobe in a patient who died after eleven years of illness at the age of 54. He postulated adaptation to diminished demand as the explanation for the thickening of the vessel wall and narrowing of the lumen, which amounted to closure in some branches of small caliber of the arteriae hypophysis superiores.

An attempt to ascertain whether the type of case which we have described is primarily psychogenic or organic may, after all, be too limited a manner of approaching the problem, man being such a complex whole. Study of any condition from only one aspect, and with but one point of view, can never reveal the whole truth.

That it is not always the anorexia which initiates this syndrome is demonstrated by our third patient. Although this woman presented most of the striking features of our other two patients and of those in the literature described as having anorexia nervosa or pituitary emaciation, she differed in the following important detail: she insisted that her appetite had always been very good but that she had vomited after almost every meal for years. This had led finally to hematemesis, of which she reported seventy instances in the course of several years. In other words, the typical clinical picture of anorexia nervosa had been produced in this case by hyperemesis nervosa.

Despite the current trend of emphasizing the psychogenic factor, Meyler [58] says, "it is a mistake to consider these people as hysterics." However, the psychologic aspects of the syndrome cannot thus simply be dismissed without more evidence.

It seems wise to concede that this strange clinical picture is as yet incompletely understood and that much further work remains to be done, particularly detailed reporting of the psychologic features in fatal pituitary cachexia and careful somatic and postmortem studies of the so-called primary psychogenic types of anorexia nervosa. Some people respond to emotional trauma by excessive food intake; certain cases of obesity result from such a mechanism. Certain obese patients take to food in the same sense that a drunkard takes to drink, namely in response to a psychic conflict; and the management of such problems, like the management of anorexia nervosa, is often most satisfactory when directed largely through psychic channels.

Owing to the uncertainties as to etiology, the practical handling of these cases has been difficult and has varied from psychoanalysis to risky, repeated implantations of animal pituitary tissue into the omentum of these patients of low resistance. How many of these unfortunate girls have been sent to tuberculosis sanatoriums, as was our first patient, who at the outset had no evidence of pulmonary tuberculosis? How many have died in psychiatric institutions classified as

55. von Noorden, Karl, and Salomon, Hugo: Handbuch der Ernährungslehre, Berlin, Julius Springer, 1920, p. 952.

56. Benedict, F. G.; Miles, W. R.; Roth, P., and Smith, H. M.: Human Vitality and Efficiency Under Prolonged Restricted Diet, Publication 280, Carnegie Institution of Washington, 1919.

57. Sheehan.[41] Sheehan and Murdock.[42]

58. Meyler, L.: Simmonds' Disease (Hypophysary Emaciation) Acta med. Scandinav. **96**: 157, 1938.

schizophrenic or depressive? Before there are as clear diagnostic methods to differentiate between anorexia nervosa and pituitary cachexia as there are to separate psychogenic polydipsia from diabetes insipidus, one should be hesitant in making a definite diagnosis. While endocrine substitution therapy is being pushed, one should not forget the probable great importance of patience, tact and kind understanding of the patient's personal problems, a therapeutic approach in which the older type of physician seems to have been superior to our highly specialized, modern physician. Déjerine and Gauckler's [6] statement that there is no way of telling if a patient will or will not get well seems worth remembering. Even though in two of our cases insulin seems to have helped, one must be cautious in the evaluation of its therapeutic effects in view of the first girl's strange gain in weight during the most active febrile stage of her tuberculous process. Although we observed no serious accident during the insulin treatment, one should be on guard for such severe reactions (Josefson,[18] Schüpbach [33] and von Bergmann [26]). Evidently the longer the patient's illness has lasted, the more difficult will be the cure. It will be even more difficult if complicated by signs of avitaminosis and food deficiency, as illustrated by our third patient with spontaneous fractures of decalcified bones and possible vitamin C deficiency. In this regard Thannhauser's [59] paper on pellagra and endocrine disturbances suggests interesting new fields of clinical investigation. In an unreported case one of us has seen early manifestations of typical pellagra in a young girl with anorexia nervosa. After she had been extremely emaciated and had resisted all efforts to make her gain weight, both conditions spontaneously subsided when she suddenly changed her mind and began to eat ravenously.

One final question should be raised, namely Is the fundamental disorder in cases of anorexia nervosa —psychic or endocrine—ever really curable, and if so what are the criteria for such a cure? Apparently full recovery, even for a few years as in case 2, is in itself not a sufficient criterion for predicting a permanent cure, even when weight is maintained at a normal level. This fact might favor the importance of the psychogenic element in the pathogenesis of anorexia nervosa as the neuroses are so notoriously liable to recurrence, even with comparatively slight psychic trauma.

SUMMARY AND CONCLUSIONS

The condition of anorexia nervosa is apparently not uncommon, although there was practically no American literature on the subject prior to 1932.

The etiology is obscure.

There is no regularly satisfactory treatment. Some patients recover seemingly spontaneously, as did one of our patients. Two of our patients seemed to improve after insulin therapy, although one of them after a relapse did not respond so strikingly to insulin on a second trial.

The criteria for cure have not been established. In one of our cases, after apparently complete recovery from both clinical and laboratory standpoints for a period of four years, amenorrhea and then edema developed without preceding significant loss of weight and following comparatively slight emotional trauma. It appears that some underlying disturbance, somatic, psychic or psychosomatic, may persist even when a patient seems to have fully recovered.

It is possible that the clinical picture of anorexia nervosa may develop somewhat as follows: Certain individuals may react to emotional conflict by developing anorexia. As a result, then, of a diminution of the normal stimulus to appetite which regular food intake produces, this anorexia may become prolonged and self perpetuating. With the consequent loss of weight all of the unusual features associated with the cases described may appear purely as a physiologic response to weight reduction and semistarvation. Why only few individuals will react to emotional conflicts in this manner (while most do not) can be explained only if certain necessary conditioning factors are assumed. What such conditioning factors are must remain in the field of speculation. Here perhaps lie the so-called primary endocrine factors. The management of anorexia nervosa is often most satisfactory when directed largely through psychic channels.

59. Thannhauser, S. J.: Pellagra und endokrine Störungen, München. med. Wchnschr. **80:** 291 (Feb. 24) 1933.

RENAL LESIONS FOLLOWING ADMINISTRATION OF HYPERTONIC SOLUTIONS OF SUCROSE

REPORT OF SIX CASES

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Intravenous administration of hypertonic solutions of sucrose has become popular within recent years for the reduction of increased intracranial pressure. Bullock, Gregersen and Kinney [1] in 1935 showed that sucrose reduced cerebrospinal fluid pressure without a secondary rise, such as followed administration of dextrose or saline solutions. The usefulness of sucrose was confirmed by Masserman [2] and by Jackson, Dickerson and Gunther.[3] The injected sucrose did not appear to metabolize or to diffuse out into the cerebrospinal fluid. The sugar was rapidly excreted by the kidneys, with a marked diuresis amounting to about four times the amount of sucrose solution injected. Toxic effects noted were slight, although patients complained of malaise and muscle pain, and a moderate leukocytosis occurred.

Helmholz [4] in 1933 noted that hypertonic solutions of sucrose given intravenously to rabbits produced marked renal lesions. One hour after a 20 per cent solution of sucrose was administered, the cells of the renal convoluted tubules began to swell. This swelling persisted for about a week. The change in the cells of convoluted tubules was a marked vacuolar degeneration. The cytoplasm became finely granular and the cells stained very lightly. Nuclear shrinkage occurred. Glomerular spaces and tubular lumens became filled

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The illustrations in this study were made by Dr. Joseph L. Scianni, artist, University of Tennessee Pathological Institute.

1. Bullock, L. T.; Gregersen, M. I., and Kinney, R.: The Use of Hypertonic Sucrose Solution Intravenously to Reduce Cerebrospinal Fluid Pressure Without a Secondary Rise, Am. J. Physiol. **112:** 82 (May) 1935.

2. Masserman, Jules H.: Effects of the Intravenous Administration of Hypertonic Solutions of Sucrose with Special Reference to Cerebrospinal Fluid Pressure, Bull. Johns Hopkins Hosp. **57:** 12 (July) 1935.

3. Jackson, Harry; Dickerson, Donald, and Gunther, Aaron: The Reduction of Intracranial Pressure in Cerebral Injury by the Intravenous Use of Hypertonic Sucrose Solution, Ann. Surg. **106:** 161 (Aug.) 1937.

4. Helmholz, H. F.: Renal Changes in the Rabbit Resulting from Intravenous Injection of Hypertonic Solution of Sucrose, J. Pediat. **3:** 144 (July) 1933.

with granular material. The changes began to subside on the seventh day, and by the fifteenth day there was restitution to a normal appearance. However, if the injections were repeated at intervals of three days or less the changes were more severe and eventually progressed to epithelial atrophy and sclerosis of the renal tissue. Following this repeated administration of sucrose there was a marked decrease in functional capacity of the kidney, as measured by the output of phenolsulfonphthalein.

Lindberg, Wald and Barker [5] verified and extended this work by studies on dogs. They described the same type of renal lesion following the administration of 50 per cent solutions of sucrose. The changes reached their maximum between the third and fifth days after injection. They emphasized the tendency to resolution of the lesion unless there was prolonged repeated administration. Hypertonic solutions of d-sorbitol, dextrose and sodium chloride failed to produce similar renal lesions.

Helmholz [4] also described one human case in which there had been a series of injections of hypertonic solutions of sucrose. The renal tubular cells were greatly swollen and pale, and the changes were similar to those present in the experimental animals. No significant change in urea clearance following a single injection of 200 cc. of 50 per cent solution of sucrose in human beings was found by Lindberg, Wald and Barker.[5]

Administration of Sucrose and Associated Renal Damage

Case	Amount of 25% Sucrose Administered (Cc.)	Number of Injections	Period of Administration (Days)	Time Before Death of Last Injection (Hours)	Characteristic Renal Changes
1	3,350	15	4	4	Very severe
2	1,750	7	4	8	Very severe
3	1,000	4	3	8	Severe
4	200	1	1	3	Moderate
5	200	1	1	11½	Moderate
6	100	1	1	12	Slight, early recognizable

The use of hypertonic solutions of sucrose was started in this hospital in the latter part of 1938. Within the last six months a peculiar type of renal tubular lesion has been noted in routine autopsies. This was so striking in some cases and so different from anything observed previously that it led to speculation as to its origin. The similarity between these changes and those described by Lindberg, Wald and Barker and by Helmholz was recognized. On examination of the clinical records it was found that the patients had received repeated intravenous injections of hypertonic solutions of sucrose. Lesser degrees of the changes were recognized, and it was found that one could correctly state, from the section of kidney tissue alone, whether or not the patient had received hypertonic sucrose during a period of several days before death. A report of six cases follows in the hope of making these changes more widely known and recognized. The amount of sucrose administered in each case and the time relations are detailed in the accompanying table.

REPORT OF CASES

CASE 1.—D. G., a Negro man aged 65, came to the hospital complaining of pain in the lumbar region, difficulty and frequency of urination, headaches and dizziness. He was found to have marked hypertension, prostatic enlargement with urinary retention, and moderate subcutaneous edema. The nonprotein nitrogen content of the blood was 166 mg. per hundred cubic centimeters. The urinary obstruction was overcome by means of a retention catheter. Hypertonic solutions of dextrose and sucrose were administered. A total of 3,350 cc. of a 25 per cent solution of sucrose was given over a four day period. There was a gradual lapse into a stuporous and then comatose condition. Death occurred three days after the last administration of sucrose.

At autopsy there was found to be fairly severe sclerosis of the arteries and arterioles, both in the kidney and elsewhere. The prostate showed benign enlargement, and there were cystitis and pyelonephritis. Terminal bronchopneumonia had occurred. On microscopic examination of the kidneys, in addition to the damage attributed to the arteriosclerosis and pyelonephritis there was a very striking change in the convoluted tubules of the cortex. These tubules stood out as patchy light staining areas. This was due to marked swelling of the cytoplasm of the lining cells. The swollen cells had a very clear cytoplasm, only a finely granular or reticular material in the cytoplasm taking the stain. Occasionally small clear vesicles or droplets appeared in the cytoplasm, and similar material was present in the lumen. Details of this lesion as it occurred in this and the following cases will be described later.

CASE 2.—D. W., a Negro man aged 33, came to the hospital because of headaches and dizziness beginning five months previously. He was found to have a blood pressure of 220 systolic, 165 diastolic, an enlarged heart and massive edema of the disk and retina with exudates and hemorrhages. The spinal fluid pressure was 300 mm. of water. The nonprotein nitrogen content of the blood was 75 mg. per hundred cubic centimeters. Hypertonic solutions of dextrose and sucrose were given intravenously. A total of 1,750 cc. of a 25 per cent solution of sucrose was administered at intervals on three of the last four days of life. The headaches continued. Nausea, vomiting and twitchings developed. The patient gradually became stuporous and comatose. Death occurred eight hours after the last dose of sucrose. The nonprotein nitrogen level was 130 mg. per hundred cubic centimeters of blood on the day of death.

At autopsy the kidneys showed the changes of severe arteriosclerosis. The convoluted tubules showed a severe generalized foamy change of the epithelial cells. The pale staining cells were so distended that many of the lumens appeared entirely closed. In some areas the cells were necrotic. The heart weighed 450 Gm. and had moderately dilated chambers, and the viscera were involved by mild chronic passive congestion. There was terminal bronchopneumonia.

CASE 3.—T. W., a Negro man aged 67, was brought to the hospital unconscious, with twitching and coldness of the lower extremities. The coma had followed a period of drowsiness and stupor noted the previous day. The temperature was 104 F., respiratory rate from 32 to 40 per minute and pulse rate 130. Death occurred on the third day without return to consciousness. A total of 1,000 cc. of a 25 per cent solution of sucrose, in 250 cc. doses, was given during these three days, the last dose being administered eight hours before death.

Autopsy showed congestion and edema of the brain but no cerebral hemorrhage. The heart weighed 350 Gm. There were marked pulmonary edema and acute bronchopneumonia. Except for a slightly granular outer surface, the kidneys appeared normal on gross examination. Microscopically the kidneys were congested and the cells of the convoluted tubules showed a severe distinctive foamy distention, comparable to that in the previous cases. Amorphous exudate was present in the tubular lumens and glomerular spaces. There was a moderate amount of sclerosis of the small vessels, with occasional fibrosed glomeruli.

CASE 4.—O. D., a white man aged 64, was admitted to the hospital unconscious and died four hours later. He had been under treatment for hypertension for several years. A single injection of 200 cc. of a 25 per cent solution of sucrose was administered three hours before death.

A recent occlusion of the left coronary artery, with a large myocardial infarction, was the cause of death. On gross examination the kidneys showed little change. Microscopically, a

5. Lindberg, H. A.; Wald, M. H., and Barker, M. Herbert: Renal Changes Following Administration of Hypertonic Solutions, Arch. Int. Med. **63**: 907 (May) 1939.

foamy swelling of the cells of the convoluted tubules was generalized. The nature of the change was the same as described in the previous cases but its severity was somewhat less. Nevertheless, many of the tubules appeared completely blocked and many cells were necrotic. The kidney shared in a general

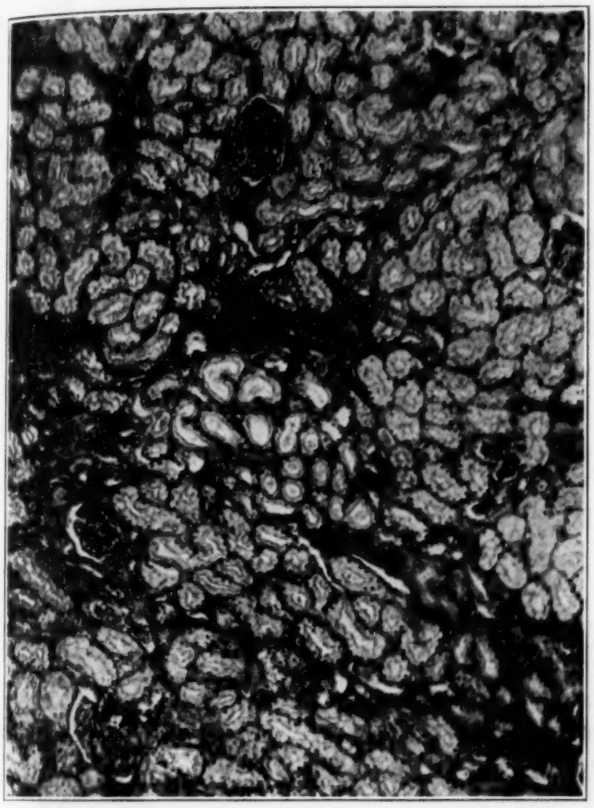

Fig. 1 (case 3).—Section of renal cortex, × 70. Swollen pale cells line the convoluted tubules. Many are without nuclei.

visceral congestion, but vascular changes were not prominent in small vessels.

CASE 5.—H. G. W., a white man aged 74, came to the hospital because of severe shortness of breath of three months' duration. Swelling of the abdomen and legs had been present intermittently for four years. Physical examination showed signs of congestive heart failure with marked edema. The nonprotein nitrogen of the blood on admission was 30 mg. per hundred cubic centimeters. The condition of the patient became progressively worse, and death occurred one and a half days after admission. A single intravenous injection of 200 cc. of a 25 per cent solution of sucrose was given eleven and one-half hours before death.

Autopsy showed mitral and aortic stenosis, with great cardiac hypertrophy and dilatation, marked chronic congestion of the viscera and generalized arteriosclerosis. The kidneys were normal on gross examination, except for slight granularity of their outer surfaces. Diffusely throughout the cortex the convoluted tubules were lined by pale swollen cells having a very foamy or vacuolated cytoplasm. All stages and grades of severity including loss of nuclei and rupture of cells could be found. Droplets and amorphous material appeared in the tubular lumens and glomerular spaces. The epithelial cells of some of the glomeruli also appeared swollen and pale staining, and a few polymorphonuclear leukocytes were present in their capillaries. The kidneys shared in the general visceral congestion.

CASE 6.—E. J. B., a white woman aged 69, became suddenly unconscious. Lumbar puncture showed blood stained fluid. Death occurred fourteen hours after she became unconscious. A single injection of 100 cc. of a 25 per cent solution of sucrose was administered intravenously about twelve hours before death. At autopsy there was found a ruptured aneurysm of the right internal carotid artery, with hemorrhage into the subarachnoid space. The kidneys showed a moderate swelling and granularity of the tubular epithelium. The characteristic pale staining foamy change of the cytoplasm was present in only one focal area.

COMMENT

In cases 1 and 2 the severe generalized lesion involving the renal convoluted tubules was inflicted as an additional burden on kidneys already badly damaged by vascular changes. In case 1 infection and obstruction also contributed to the renal damage. Cases 1, 2 and 3 all showed the results of repeated administration of hypertonic solutions of sucrose over periods of three and four days. In each instance the renal lesion was generalized and severe, with distinctive and easily recognizable characteristics. Case 4 reveals the rapidity with which the characteristic tubular changes are brought about, being well developed three hours after the sucrose was administered. It is evident from cases 4 and 5 that a single dose of 200 cc. of a 25 per cent solution of sucrose will result in marked lesions. Even after 100 cc. slight but definite lesions appear, as illustrated in case 6.

Two groups of cases were selected to act as controls. In each case sections of the kidneys were searched for lesions such as are described in the reported cases. The first group, consisting of fifty adults, were examined

Fig. 2 (case 2).—Section of renal cortex, × 150. Note granularity and foamy appearance of swollen tubular cells. Some of the lumens are greatly narrowed. Amorphous material and rounded droplets are present in some of the lumens.

post mortem before the use of sucrose was started in this hospital. The second control group comprised twenty patients who had indications for the administration of hypertonic solutions but for whom sucrose had not been used. Many of these had been given hyper-

tonic solutions of dextrose. Lesions in the kidneys similar to those which follow intravenous administration of hypertonic solution of sucrose were found in none of these control cases. Among cases coming to autopsy within a few days of the administration of a hypertonic solution of sucrose, there was only one in which the characteristic renal lesion was not found. In this instance there were marked autolytic changes in the kidneys, and the lesion due to sucrose, if present, was entirely masked.

Intravenous administration of hypertonic solutions of sucrose produces renal lesions of peculiar nature, their apparent specificity and easy recognition being striking. While the series of cases reported here is small, there is enough variety of dosage and time between administration and death that some information may be gained regarding the succession of changes which develops. The earliest and mildest lesion appears to be a slight swelling and granularity of the cytoplasm of the cells lining the convoluted portions of the tubules. The swelling of the epithelial cells progresses and the cytoplasm becomes very pale, so that within three hours the appearance is quite changed. A lumen is frequently not visible between the swollen cells. At this time the cytoplasm contains very fine granulations. The granulations may soon appear as a very fine reticulum. Later, small round clear vesicles or droplets appear in the cytoplasm and apparently are extruded into the tubular

Fig. 3 (case 2).—Section of renal cortex, × 150. Accumulation of leukocytes in glomeruli is shown here, as well as the characteristic tubular lesion.

lumen, or rupture of the cell and desquamation of its contents into the lumen occur. The basement membranes are not involved. The nuclei show little change until the severer degrees of damage are present, when they begin to fade, become shrunken and pyknotic and may entirely disappear. These severe changes in the tubular epithelium involve the convoluted portions of practically all tubules to a similar degree in any one case.

The glomeruli also show some changes, particularly after administration of large amounts of hypertonic solu-

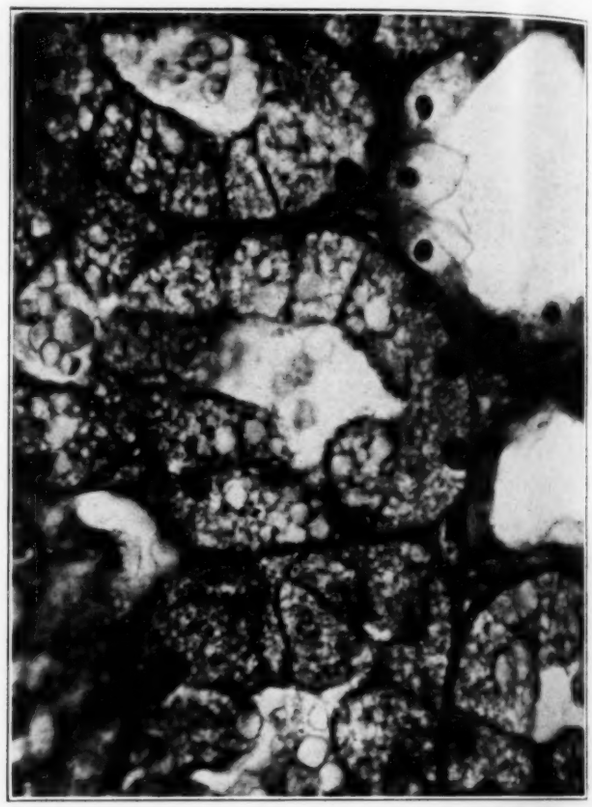

Fig. 4 (case 2).—Section of renal convoluted tubules, × 550. Note details of the severe changes in tubular epithelium. Droplets of various sizes are collecting in the swollen granular cytoplasm. Some of the droplets are being extruded from the cells, and similar droplets are evident in the lumens. Many of the affected cells have no visible nuclei.

tions of sucrose by repeated doses at short intervals. The capillaries of the glomerular tufts are congested, and in some a few leukocytes collect. The nucleus and cytoplasm of the epithelial cells of the tufts become larger and more prominent, appearing swollen and granular. This change does not occur to the marked degree seen in the tubular cells. Later some of the glomeruli appear shrunken and the capsular space is correspondingly increased. Clear droplets and amorphous pale eosin staining material appear in the glomerular spaces and the lumens of the convoluted tubules.

The nature of the material in the swollen tubular cells was not determined. Staining by sudan IV for fat produced negative results. The tissues were not suitably fixed for the demonstration of glycogen.[5a]

After injection of sucrose into the blood stream, the sugar is not metabolized and probably but little diffusion occurs into the tissues. The sucrose is almost completely excreted by the kidneys within a few hours by the process of glomerular filtration. Clearance of sucrose from the blood has been shown to be similar to that of urea or creatinine and is comparably decreased in renal diseases with the exception of nephrosis.[6] The

5a. In cases studied since this manuscript was submitted, no glycogen could be demonstrated in involved tubular cells by Best's carmine stain.

6. Winkler, Alexander W., and Parra, Jose: The Measurement of Glomerular Filtration: The Creatinine, Sucrose and Urea Clearances in Subjects with Renal Disease, J. Clin. Investigation **16:** 869 (Nov.) 1937.

mechanism by which sucrose damages the tubular cells is not known. It seems probable that passage of sucrose through the tubular lumen, possibly with some slight reabsorption, may cause disturbance in the water balance of the individual tubular cells. The marked diuresis resulting from injection of sucrose may be due in some degree to interference with the reabsorptive function of the tubules as a result of this damage.

No conclusions as to the effect of the lesion on renal function can be drawn from these cases. The observation of Helmholz [4] and of Lindberg, Wald and Barker [5] suggest that, in experimental animals, function is not diminished unless hypertonic solutions of sucrose are repeated several times without adequate intervals for recovery. Since most tests of renal function will measure only very gross changes in the efficiency of a normal kidney, it cannot be concluded on the basis of these tests alone that no functional damage results. It seems probable that there is significant change in the efficiency of tubular function, considering the degree of morphologic change in the tubules and its widespread nature. Until more information is obtained concerning this,

Fig. 5 (case 2).—Convoluted tubules, × 550. Here the individual cells have lost their definite outlines. Vesicular and amorphous material is prominent in the lumens.

it seems inadvisable to inject hypertonic solutions of sucrose into individuals with renal arteriosclerosis, chronic nephritis or other types of renal damage. In any case, repetition of administration should be avoided, except at intervals of several weeks.

SUMMARY

1. In six cases distinctive renal lesions were found after the intravenous administration of hypertonic solutions of sucrose. Similar lesions have been observed in experimental animals after injection of sucrose.

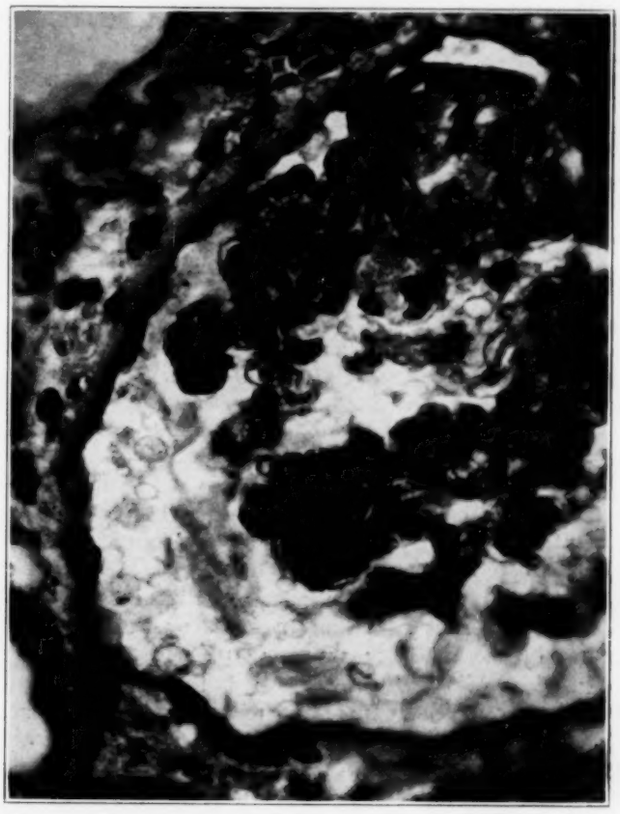

Fig. 6 (case 2).—Glomerulus, × 550. There is shrinkage of the tuft, with amorphous material and clear droplets in Bowman's space.

2. The lesion is characterized primarily by extreme foamy swelling of the lining cells of the renal convoluted tubules. The change may progress to death of the cells.

3. The administration of hypertonic solutions of sucrose to patients with renal damage is inadvisable. Large or repeated intravenous doses of sucrose should be avoided.

Diabetic Coma.—All these causes of diabetic coma have this in common: They lead to the body's inability to burn enough sugar for proper combustion of the fats furnishing body heat. As has been noted, fats are substances with even numbers of carbon atoms in their molecules which, when not completely burned, form ketones or organic acids; carbohydrates (sugars) supply the heat which is needed for the complete combustion of these fats within the body, and insulin makes it possible for the carbohydrates to burn. The cycle, therefore, is obvious: no insulin, no burning of sugars; no sugar combustion, no complete fat combustion. When fats do not burn completely, they leave this harmful acid residue, and the first stage of diabetic coma is the resulting body acidosis. Ketones may appear for several reasons, all of which have one thing in common: An insufficient amount of carbohydrate is being burned for the amount of fat metabolized. Ketosis may result from starvation or from exclusively fat diets, as well as from diabetes.—Pollack, Herbert, Modern Diabetic Care, New York, Harcourt, Brace and Company, 1940.

SOLUBLE IODOPHTHALEIN IN TREATMENT OF CARRIERS OF TYPHOID-PARATYPHOID GROUP

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The management of carriers of the typhoid-paratyphoid group of bacteria presents a difficult problem. In spite of many attempts to free the carriers from bacteria there is no known method which will accomplish this task with a reasonable degree of success.

Older reports as to successful treatment of such carriers with various drugs have not fulfilled expectations. In the most extensive review of this subject in recent years (Browning [1]) the conclusion is reached that drug treatment, chemotherapy, physical therapy, measures aimed at alteration of the reaction of the flora of the intestine and vaccine therapy have all proved ineffective.

It is not surprising, therefore, that most public health agencies assume a rather conservative attitude toward such carriers. In the state of Illinois carriers are prevented from engaging in certain occupations such as food handling and dairy work and are supervised in order to avoid the spread of the disease. Over 300 typhoid carriers have been detected in recent years and are now under supervision in Illinois according to a report by the state department of public health.[2]

In view of the futility of drug therapy there has been an increasing tendency in recent years to perform cholecystectomy on carriers of the typhoid-paratyphoid group. Cholecystectomy has effected cure in 75 per cent of the cases when the gallbladder was found to be the site of infection.[1]

There is indeed much evidence for the view that the carrier state is maintained by the gallbladder. Such a gallbladder seems to be acting as a test tube, containing the bile medium in which the bacteria propagate without necessarily affecting the gallbladder itself (Garbat [3]). This opinion is supported by experiments with rabbits and other animals, in which it has been demonstrated that after intravenous injection of typhoid bacilli the organisms are excreted by the liver and may soon appear in the bile of the hepatic duct (Meyer, Neilson and Feusier [4]).

The value of cholecystectomy in the treatment of typhoid carriers is well established. This is particularly true when, through the use of duodenal drainage, the duodenal fluid is found to contain typhoid bacilli (Bigelow and Anderson [5]). Yet there exists considerable and justifiable hesitancy on the part of the physician to submit an otherwise healthy individual to cholecystectomy, when frequently enough the gallbladder after removal appears to be normal.

For this reason an attempt was made to cure a carrier of Bacterium paratyphosum A by conservative procedures before considering surgical treatment. After all other conservative measures, including sulfanilamide, had failed, a surprising success was noted with soluble iodophthalein.

This dye is commonly used in x-ray visualization of the gallbladder and has previously been suggested for the medication of typhoid carriers (Onodera, Murakawa and Liu [6]). However, the results were not uniformly satisfactory. It is believed that the mode of administration plays a great part in the final success.

While no definite claim can be made as to the permanent success and value of a suggested treatment on the basis of a single case, it is our purpose in this paper to call attention to this form of treatment of carriers of the typhoid-paratyphoid group and to report the investigation of the possible bactericidal properties of soluble iodophthalein.

REPORT OF CASE

Miss E. M., a registered nurse aged 23, was admitted to the Michael Reese Hospital with a history of diarrhea for the past seven months. The stools were watery and light, containing a great deal of mucus. There were abdominal cramps, frequently associated with the bowel movements. The evacuations sometimes numbered ten daily. While the acute symptoms had almost subsided before hospital admission, the patient was asked to enter the hospital because a bacteriologic examination of the stools had revealed the presence of Bacterium paratyphosum A.

Physical examination did not reveal anything significant. The patient appeared somewhat underweight but had not lost weight recently. The heart and lungs were normal, the abdomen was slightly distended and there was some tenderness over the ascending and descending colon. Rectal examination was negative. There was no elevation of temperature at any time during the hospital stay. Repeated blood counts, urine and blood pressure examinations were consistently normal.

The patient was placed on a regimen of low residue diet and bed rest. Daily specimens of stool were sent to the laboratory and in each instance paratyphoid A bacilli were isolated. An autogenous vaccine was prepared. The patient received increasing doses of the vaccine every second day hypodermically, but there was no change in the bacteriologic flora of the stools. On three separate occasions the patient's blood serum was examined for paratyphoid A agglutinins with negative results.

A further attempt was made to eradicate the bacilli with sulfanilamide. Over a period of eight days, 200 grains (13 Gm.) of sulfanilamide was administered orally. However, the bacillary excretion remained constant. Finally, large doses of bismuth subcarbonate as well as kaolin were given without curative effect.

Duodenal drainage revealed, by direct smear, the presence of gram-negative bacilli. An attempt to culture them on blood agar, Endo's agar and various broths failed.

After several days 4 Gm. of soluble iodophthalein was administered orally in the form used for x-ray visualization of the gallbladder. On the following day bacteriologic examination of the stool failed to reveal the organisms. Administration of the dye was repeated twice in the next six days. Subsequent daily stool specimens remained negative for Bacterium paratyphosum A.

The patient was discharged with the instruction to take the dye once a week for one month. She was kept under observation for the following seven months, and repeated stool examinations during this period were consistently negative.

BACTERICIDAL TESTS

Soluble iodophthalein administered orally to the carrier of Bacterium paratyphosum A was so surprisingly

From the medical and bacteriologic department of the Michael Reese Hospital.

1. Browning, C. H.: Chronic Enteric Carriers and Their Treatment, Medical Research Council, Special Report Series, No. 179, London, His Majesty's Stationery Office, 1933.
2. Statement of Department of Public Health, State of Illinois, Chicago M. Soc. Bull. **42:** 8 (July 1) 1939.
3. Garbat, A. L.: Typhoid Carriers and Typhoid Immunity, Monograph 16, New York, Rockefeller Institute for Medical Research, 1922.
4. Meyer, K. F.; Neilson, N. M., and Feusier, M. L.: The Mechanism of Gallbladder Infections in Laboratory Animals, J. Infect. Dis. **28:** 456 (May-June) 1921.
5. Bigelow, G. H., and Anderson, G. W.: Cure of Typhoid Carriers, J. A. M. A. **101:** 348 (July 29) 1933.
6. Onodera, N.; Murakawa, G., and Liu, S.: Ueber eine neue Behandlung von Typhusbazillentraegern, Deutsches Arch. f. klin. Med. **171:** 503, 1931.

effective in eradicating the bacteria from the bile and stool that it seemed probable that the dye must exert a strongly bactericidal action on paratyphoid A bacilli. Accordingly a series of in vitro tests were performed to determine the bactericidal and bacteriostatic effect of the dye.

1. The initial concentration of the dye was 10 per cent in sterile distilled water. Serial dilutions ranging from 1:2 through 1:2,048 were made with sterile distilled water. Each test tube was inoculated with 0.01 cc. of a twenty-four hour culture of Bacterium paratyphosum A in broth. At intervals of one minute, three minutes, five minutes, thirty minutes, one hour and twenty-four hours transfers from each dilution were streaked on Endo's agar. As controls, cultures were made from the paratyphoid A bacilli, the distilled water and the dilutions of uninoculated dye. All the subcultures except those from the distilled water and the uninoculated dye gave luxuriant growth on Endo's agar.

2. On the chance that the bile in the gallbladder enhanced the bactericidal action of the dye in vivo, the test was repeated with the modification that 1 cc. of sterile bile was added to each dilution of the dye before inoculation with paratyphoid A bacilli. There was no apparent inhibition of bacterial growth in any of the dilutions, even after the twenty-four hour exposure to the dye.

3. In the third series of tests the concentration of the dye was increased to 30 per cent and no dilutions were made. Instead, the bacterial dose was progressively decreased by adding three loops of twenty-four hour broth culture to the first test tube, three loops from the first tube to the second, and so on through twelve tubes. At intervals of one minute, three minutes, five minutes, twenty minutes, one hour, two hours and twenty-four hours transfers from each tube were streaked on Endo's agar. Subcultures from the first two tubes, those in which the inoculum was comparatively heavy, grew even after twenty-four hours of exposure to the dye. The tubes containing the third and fourth dilution of inoculum gave diminished growth after one hour's exposure. Transfers from the other dilutions of inoculum did not grow. A control set of tubes containing broth instead of dye and inoculated with corresponding doses of paratyphoid A bacilli supported growth in all cases. This series using small inoculations of paratyphoid A bacilli and the concentrated dye indicated a possible slight bactericidal and bacteriostatic property of soluble iodophthalein.

4. Since our results did not correspond to those reported by Onodera, Murakawa and Liu,[6] it was decided to repeat the tests using their exact procedure with Bacterium typhosum, but using our culture of Bacterium paratyphosum A. A series of test tubes containing 5 cc. of glycerin gall bouillon with various concentrations of the dye (0.5, 1, 2, 3, 4, 5 and 6 per cent) were inoculated with a loop of twenty-four hour culture of paratyphoid A in broth. After incubation periods of one, three, five, seven, ten, twelve and twenty-four hours, respectively, one loop of culture medium was transferred from each test tube and streaked on plain agar. There was luxuriant growth in all cultures taken through the ten hour period. Subcultures from the twelve and twenty-four hour periods in the higher concentrations of the dye (from 4 to 6 per cent) were diminished by from 20 to 25 per cent, according to colony counts. The plate cultures were further incubated for five days and showed no material change, indicating that the action of the dye was for the most part bactericidal and only slightly bacteriostatic. In our hands the bactericidal action was not as strong as that reported by Onodera, Murakawa and Liu, who obtained no growth after twelve and twenty-four hours of exposure to the dye in from 4 to 6 per cent concentration.

COMMENT

The case described was that of a carrier of Bacterium paratyphosum A. The bacilli were found consistently in repeated stool examinations. The patient did not appear acutely ill and did not offer any clinical evidence of acute enteric disease except for some tenderness over the region of the colon and frequency of bowel movements.

A series of conservative measures such as vaccine treatment and sulfanilamide, bismuth and kaolin medication failed to exert any influence on the bacterial flora. Duodenal drainage revealed the presence of gram-negative bacilli which failed to grow in culture.

Soluble iodophthalein has been reported as having been administered to typhoid carriers (Onodera, Murakawa and Liu[6]). The results were not too encouraging; of seven patients only three were free from bacilli after a month's observation. However, in these cases soluble iodophthalein was given by the intravenous route and only on one or two occasions. It appeared to us that both the oral route and frequent doses might offer much better results. In that way the dye would enter the duodenum in rather concentrated form and exert its action on the bacilli present in the duodenal contents. Absorption of the dye from the intestine and its concentration in the gallbladder might sterilize the contents of the gallbladder. It also seemed to us that the intestinal absorption of the dye and its entry into the liver by way of the portal vein might be more likely to imitate the normal physiologic mechanism. On the other hand, if the intravenous route was chosen the dye would enter the liver by way of the hepatic artery. In this way it might enter the gallbladder in less concentrated form. Certainly the intravenous route does not offer any direct action on bacilli present in the duodenum, which is the case in oral administration.

The results of our bacteriologic study would indicate that the action of soluble iodophthalein on Bacterium paratyphosum A cannot be explained entirely on the basis of its bactericidal action. Growth of Bacterium paratyphosum A in the in vitro tests can be destroyed by the dye only in such concentrated solutions as would probably not occur in the human organism. It is therefore postulated that some reaction on the part of the tissues—perhaps on a fermentative, chemical or other unrecognized basis—plays a fundamental part in destroying the bacteria.

SUMMARY AND CONCLUSION

1. A series of conservative measures including the use of sulfanilamide failed to render the stools of a carrier of Bacterium paratyphosum A free from these bacilli.

2. The oral administration of soluble iodophthalein was followed by immediate disappearance of the paratyphoid A bacilli from the stool. Repeated stool

examinations extending over a seven months observation period remained consistently negative for these organisms.

3. The results of a bacteriologic study in vitro as to the bactericidal action of soluble iodophthalein on the bacilli of the paratyphoid group did not entirely explain the curative action in a human carrier.

RETINITIS PIGMENTOSA AND ASSOCIATED NEUROPSYCHIATRIC CHANGES

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Nettleship [1] in 1907 was the first to indicate the extent of retinitis pigmentosa in the population when he reviewed the records of 100 patients whom he had personally observed and of 1,600 other patients concerning whom he was able to secure adequate descriptions. He noted other disturbances associated with retinitis pigmentosa but particularly emphasized "degenerative" disturbances of the central nervous system associated with congenital somatic defects. Males predominated in his group (61 per cent), in Cockayne's [2] (61 per cent), in Bell's [3] (55.6 per cent) and in ours (61 per cent).

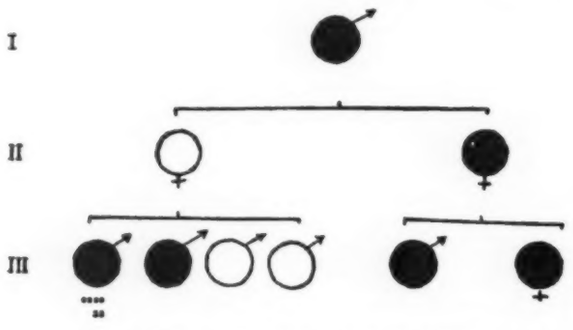

Chart 1.—Three generations of retinitis pigmentosa.

We have studied forty-one patients with retinitis pigmentosa and found that the retinas were clearly involved in each of them. Thinning of the retinal vessels was common, with deposits of black pigment usually in the periphery and following the vessels. At times it covered the central part of the retina. Often it was of the "spider-web" configuration, in some patients it took the form of linear streaks, in others it was granular, and in still others it consisted of massive patches. The optic disks in some had a normal appearance; often the nerve head had a yellow red tinge, and occasionally one saw optic atrophy. Verhoeff [4] advances the theory of abiotrophy to explain the essential retinal lesion, which appears to be a degeneration of the neuroepithelium of the retina.

Our forty-one patients come from thirty-two families and thirty-three sibships; eighteen of these families have more than one member affected with this eye difficulty. Consanguinity is present in two families (6 per cent), and this incidence is obviously greater than occurs in the general population. The patients' ages range from 11 to 69 years, the majority being over 30.

The genetic factors in this disease are important and have been stressed by others. Examination of the literature and of our cases makes it clear that one must deal with many variables when studying the genetics of retinitis pigmentosa. Madge Macklin [5] mentions eleven types. Wibaut [6] believes there are two types, as does Haldane.[7] Macklin [5] lists five instances of a dominant mode of inheritance and eighteen instances of a recessive mode. In three affected families the disease seemed to be inherited as a sex-linked recessive. Wibaut [6] divides the inheritance of retinitis pigmentosa on the basis of the presence or absence of associated changes. He concludes that when retinitis pigmentosa is associated with other lesions it is inherited in a recessive manner, but when it is without complications it is inherited as a dominant. Haldane [8] too gives some evidence for a dominant form of inheritance, but he has described also a recessive form which is not associated with deafness and not completely sex linked.

It is unlikely that this malady is inherited in four different ways. Two recent studies furnish a simpler explanation. Dr. Macklin,[9] in a genetic study of the Laurence-Moon-Biedl syndrome (a disease closely related to retinitis pigmentosa in which there are usually retinitis pigmentosa, obesity, polydactylism and mental deficiency), postulates that this syndrome "may be dependent upon two factors, both of which are necessary before the disease becomes evident, one of which is dominant and autosomal, and the other sex-linked recessive." Penrose [10] suggests that the Laurence-Moon-Biedl syndrome, like some other inherited diseases, may appear in different forms. Classically it is homozygous with polydactylism, obesity, mental deficiency and retinitis pigmentosa. However, in its heterozygous form digital anomalies are common but obesity is but rarely present.

Although sex linkage is suggested by the predominance in this series of males over females affected, it cannot be the only factor responsible. Macklin [9] has emphasized the genetic fact that, "before a daughter can have a sex-linked recessive disease, it is necessary that her father have it also." In our group the father was affected in only three families, and in one of these families both parents were affected.

Although deafness associated with retinitis pigmentosa was mentioned by Nettleship, it has never received adequate emphasis. In studying the genetics of retinitis pigmentosa, Julia Bell [3] noted an incidence of 10.4 per cent deafness or deaf-mutism. But it increased to 74.3 per cent when the pedigrees affected with deafness were considered separately. That is, if one considers solely families of retinitis pigmentosa with associated deafness, the probable related incidence of associated deafness increases sevenfold in the relatives. She therefore concludes that "whenever deafness is associated with reti-

Read before the American Neurological Association, Atlantic City, N. J., June 6, 1939.
The Neurological Service of Bellevue Hospital, the New York Association for the Blind and the Hebrew Association for the Deaf, all of New York, gave permission to use this case material.

1. Nettleship, E.: Roy. London Ophth. Hosp. Rep. **17**: 1, 151, 333. 1907-1908.
2. Cockayne, E. A.; Krestin, David, and Sorsby, Arnold: Quart. J. Med. **4**: 93 (April) 1935.
3. Bell, Julia: Retinitis Pigmentosa and Allied Diseases, London, Cambridge University Press, 1922.
4. Verhoeff, F. H.: Arch. Ophth. **5**: 392 (March) 1931.
5. Macklin, Madge T.: Medicine **14**: 1 (Feb.) 1935.
6. Wibaut, F.: Klin. Monatsbl. f. Augenh. **87**: 298, 1931.
7. Haldane, J. B. S.: Ann. Eugenics **7**: 28 (June) 1936.
8. Haldane, J. B. S.: J. Genetics **31**: 317 (Oct.) 1935.
9. Macklin, M. T.: J. Hered. **27**: 97 (March) 1936.
10. Penrose, L. S.: Ann. Eugenics **7** (part 1): 1 (June) 1936; J. Ment. Sc. **84**: 693 (Sept.) 1938.

nitis pigmentosa the link is a close one." Jenkins and Poncher [11] are of the opinion that this association is on the basis of "linkage of the genes." Eleven of our patients are deaf-mutes; in seven others, deafness was a late development. Therefore, in our series 44 per cent had associated deafness.

Many of our patients presented other interesting somatic and psychologic variations. Those with blindness alone usually seem to make a happy social adjustment. If deafness precedes this blindness there may be paranoidal personality changes. Two of our patients are mentally retarded; clinically they appear to be morons. One patient is schizophrenic with auditory hallucinations. Two others have convulsive disorders. Associated changes such as persistent amenorrhea, polydactylism, obesity and thyrotoxicosis were observed in this group.

Other investigators have emphasized the general nature of this disturbance. Dax [12] demonstrated that the blood and urine of eight adult mental defectives with retinitis pigmentosa contained a substance (probably of pituitary origin) capable of dispersing melanosomes of a frog after injection. Takahashi [13] investigated the liver function in twelve cases of retinitis pigmentosa and reported it abnormal in every one.

Examination of our cases makes it evident that retinitis pigmentosa is only a sign of a more generalized

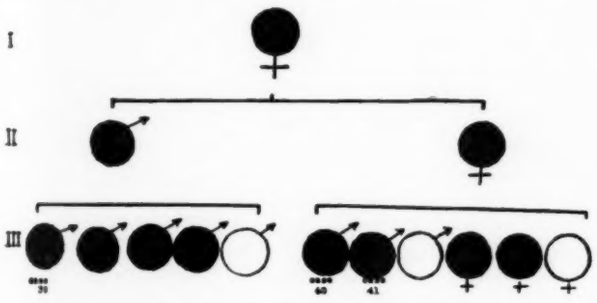

Chart 2.—Three generations of retinitis pigmentosa.

disturbance. This may be one reason for the lack of conformity of the various genetic theories. Disturbance in the development of the eye exerts a great effect on other body organs [14] and may be one explanation for some of the varied associated changes we found.

SUMMARY

In forty-one cases of retinitis pigmentosa:

1. Three fifths of the patients are males.

2. In most families more than one member is affected.

3. Two fifths of the patients are deaf.

4. Other somatic and psychologic defects are commonly found.

5. In spite of their visual disturbance these patients make a happy social adjustment, but if deafness precedes their blindness they may have mild paranoid changes.

6. There is biologic evidence of a general body metabolic disturbance in patients suffering with retinitis pigmentosa.

410 East Fifty-Seventh Street—25 West Fifty-Fourth Street.

11. Jenkins, R. L., and Poncher, H. G.: Pathogenesis of the Laurence-Biedl Syndrome, Am. J. Dis. Child. **50:** 178 (July) 1935.
12. Dax, E. C.: Brit. J. Ophth. **22:** 345 (June) 1938.
13. Takahashi, T.: Arch. f. Ophth. **116:** 143, 1925.
14. Stockard, C. R.: Am. J. Anat. **28:** 115 (Jan.) 1921.

PROSTIGMINE IN THE TREATMENT OF PERIPHERAL CIRCULATORY DISTURBANCES

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In treating peripheral circulatory disturbances, one of the most important approaches is to overcome the vasospasm which is the prime cause in the vasospastic form of vascular disturbances and an important factor in the occlusive forms. A number of medicinal products and surgical procedures have been advocated to overcome this factor and thereby aid the development of a collateral circulation. Chief among the former are acetylcholine, acetyl-beta-methylcholine chloride, the theobromine derivatives and papavarine.

Both acetylcholine and acetyl-beta-methylcholine chloride cause some peripheral arterial dilatation when given subcutaneously and in the case of the latter when it is given in large doses by mouth. My associates and I have found, however, that the action of these drugs is transitory and is not sustained for any appreciable length of time. Furthermore, the marked drop in the blood pressure, the sweating and the salivation that result when the latter is administered subcutaneously are sufficiently severe to militate against the clinical use of the drug. In an effort to avoid these side actions, acetyl-beta-methylcholine chloride has been administered by iontophoresis. Our results with this method of administration have not been satisfactory. Theobromine derivatives in our hands have also failed to produce notable peripheral vasodilatation. Papaverine hydrochloride has given us excellent results in some cases of acute vascular spasm following embolism and in ergot poisoning, but it has had very little effect in the cases with chronic vasospasm.

With regard to the surgical procedures, we have had good results in these cases with sympathetic ganglionectomy and with paravertebral alcohol injections into the sympathetic chains. These measures, however, are radical and although they are efficacious are not suitable for all cases. A more efficient conservative or medical means of producing the same effect would of course be a great help with this class of patients.

The peripheral blood vessels are innervated by two sets of nerves, the sympathetic and the parasympathetic, which are primarily antagonistic in their action. The sympathetic fibers produce vasoconstriction and the parasympathetic fibers produce vasodilatation. It has been shown that various chemical changes occur at the autonomic nerve ends and that the resulting chemicals, adrenergic in the case of the sympathetic nerve ends and cholinergic in the case of the parasympathetic nerve ends, cause the visceral responses. In addition to these chemical changes, Loewi and Navratil [1] and Stedman and his co-workers [2] have demonstrated recently that a normally present esterase, termed by Stedman cholinesterase, inhibits the action of the cholinergic substance and thus indirectly makes the action of the parasympa-

From the Peripheral Circulatory Clinic and the Cardiovascular Department of the Michael Reese Hospital and the Division of Surgery, Northwestern University Medical School.

1. Loewi, O., and Navratil, E.: Ueber humorale Uebertragbarkeit der Herznervenwirkung: Ueber das Schicksal des Vagusstoffs, Arch. f. d. ges. Physiol. **214:** 678, 1926.

2. Stedman, Edgar, and Stedman, Ellen: Studies on the Relationship Between Chemical Constitution and Physiological Action: The Inhibitory Action of Certain Synthetic Urethanes on the Activity of Liver Esterase, Biochem. J. **25:** 1147 (Nov. 4) 1931. Stedman, Edgar; Stedman, Ellen, and Easson, L. H.: Choline-Esterase: An Enzyme Present in the Blood Serum of the Horse, Biochem. J. **26:** 2056 (No. 6) 1932.

thetic nervous system intermittent. No antagonist at present known operates in a similar manner on the adrenergic substances.

In 1918 Führer [3] demonstrated that physostigmine acted synergistically with acetylcholine to increase its parasympathetic stimulating properties. Later, Loewi and Navratil [1] and Stedman and his associates [2] showed that specifically physostigmine inhibited the cholinesterase and thus permitted the unimpaired action of the acetylcholine present.

the esterases was greater than that of physostigmine. Myerson [8] and his co-workers studied its parasympathetic effect on various organs. All investigators found that the drug was safe within certain limitations and that it had fewer untoward by-effects than physostigmine. Since then it has been used successfully in the treatment of postoperative intestinal atony [9] and in myasthenia gravis.[10]

It seemed to us from these facts that theoretically prostigmine should produce vasodilatation and so might

Results of Prostigmine Treatment

Name	Age	Sex	Digital Skin Temperature: Before Prostigmine, C.	Digital Skin Temperature: 1½ Hr. After ½ Mg. Prostigmine Subcut., C.	Walking Distance: Before Prostigmine Blocks	Walking Distance: After Prostigmine Blocks	Average Number Attacks Vasospasm Daily: Before Prostigmine	Average Number Attacks Vasospasm Daily: After Prostigmine	Dosage, Mg. Daily	Duration of Treatment	Comment
Thrombo-angiitis Obliterans											
1. M. G.	65	♂	25.0	27.2	2.3	2.3	.....	.....	60	8 wk.	No improvement
2. S. H.	44	♂	24.2	26.8	1	1	.....	.....	60	12 wk.	No improvement
3. W. W.	41	♂	24.6	32.2	½	10	.....	.....	45	5 wk.	Improved
4. S. K.	43	♂	23.4	25.8	1	½	.....	.....	45	12 wk.	No improvement
5. B. B.	34	♂	24.8	29.2	3	5	.....	.....	45	4 wk.	Improved
6. M. O.	56	♂	26.0	28.4	½	4	.....	.....	45	8 wk.	Improved; ulcer on toe healed
7. W. S. A.	38	♂	26.0	29.6	1½	3½	.....	.....	45	8 wk.	Improved
8. J. S.	40	♂	24.2	30.4	1	8	.....	.....	45	6 wk.	Improved
9. J. G.	67	♂	22.0	22.4	½	½	.....	.....	45	8 wk.	Not improved
10. A. F.	44	♀	24.8	30.0	1	4	.....	.....	60	4 wk.	Improved; ulcers on fingers healed
11. D. W.	32	♂	27.4	31.2	4	8	.....	.....	45	4 wk.	Improved
Arteriosclerosis											
1. M. P.	60	♀	25.2	26.4	½	½	.....	.....	60	8 wk.	No improvement
2. S. C.	56	♂	24.8	28.2	1	4	.....	.....	45	12 wk.	Improved
3. A. W.	66	♀	23.8	23.6	½	½	.....	.....	45	8 wk.	No improvement
4. H. S.	58	♀	25.6	26.4	1	1	.....	.....	45	8 wk.	No improvement
Raynaud's Syndrome											
1. H. F.	50	♀	23.4	32.8	....	....	4-6	0-1	45	1 yr.	Improved; angina
2. M. R.	31	♀	25.2	31.6	....	....	1-2	0	45	1 yr.	Improved
3. G. P.	40	♀	27.6	31.4	....	....	1-10	1-10	120	8 wk.	No improvement
4. A. F.	50	♀	28.2	30.8	....	....	2-4	1-6	60	8 wk.	No improvement
5. L. B.	54	♀	25.4	29.2	....	....	4-8	1-2	45	6 mo.	Scleroderma improved
6. M. E.	42	♀	25.2	28.4	....	....	6-8	6-8	60	1 mo.	No improvement; angina
7. M. S.	44	♂	28.2	30.4	....	....	1-2	0-1	45	3 mo.	Improved; previous ganglionectomy
8. S. H.	45	♀	26.4	31.2	....	....	1-2	0	45	2 mo.	Improved
9. M. M.	24	♀	24.0	29.8	....	....	2-4	0	45	1 mo.	Improved
Acrocyanosis											
1. B. C.	14	♂	20.4	26.6	....	....	Cold	Warm	45	6 mo.	Color unchanged
2. N. S.	16	♀	24.2	30.4	....	....	Cold	Warm	30	6 mo.	Color normal during treatment
3. W. B.	18	♂	24.0	30.0	....	....	Cold	Warm	45	1 yr.	Color unchanged
4. M. G.	66	♂	22.8	31.4	....	....	Cold	Warm	45	1 yr.	Color unchanged
5. J. R.	58	♂	25.2	26.4	....	....	Cold	Cold	60	3 mo.	No improvement
Acute Vascular Occlusions											
1. M. Q.	74	♀	Iliac embolus 4 days, cyanosis to midthigh				.....	.....	..	.....	Slight improvement
2. J. H.	68	♂	Femoral thrombosis, cyanosis to knees				.....	.....	..	.....	Improved; gangrene of toes only

Prostigmine (the dimethyl carbamic ester of m-oxyphenyltrimethylammonium methylsulfate) [4] is a synthetic drug which acts pharmacologically like physostigmine, as shown by White and Stedman [5] and by Aeschlimann and Reinert.[6] Straub and Scholz [7] demonstrated that the inhibitory action of prostigmine on

be useful in the treatment of peripheral circulatory disturbances. With this in mind we studied the effect of prostigmine on the peripheral blood vessels.[11] We found that when administered either subcutaneously or orally it produced a vasodilatation similar to the vasodilatation following peripheral nerve anesthetization and sympathetic ganglionectomy and that the resulting eleva-

3. Führer, H.: Untersuchungen über den Synergismus von Giften: Die chemische Erregbarkeitssteigerung glatter Muskulatur, Arch. f. exper. Path. u. Pharmakol. **82:** 51, 1918.

4. The prostigmine used in this study was supplied by Hoffmann-La Roche, Inc., Nutley, N. J.

5. White, A. C., and Stedman, E.: On Physostigmine-like Action of Certain Synthetic Urethanes, J. Pharmacol. & Exper. Therap. **41:** 259 (March) 1931.

6. Aeschlimann, J. A., and Reinert, Marc: The Pharmacological Action of Some Analogues of Physostigmine, J. Pharmacol. & Exper. Therap. **43:** 413 (Nov.) 1931.

7. Straub, W., and Scholz, J.: Versuche uber den Vagusstoff, Arch. f. Exper. Path. u. Pharmakol. **182:** 331, 1936.

8. Myerson, Abraham: Human Autonomic Pharmacology: Theories and Results of Autonomic Drug Administrations, J. A. M. A. **110:** 101 (Jan. 8) 1938.

9. Carmichael, E. A.; Frazer, F. R.; McKelvey, D., and Wilkie, D. P. D.: The Therapeutic Action of Prostigmine, Lancet **1:** 942 (May 5) 1934.

10. Walker, M. B.: Case Showing the Effect of Prostigmine on Myasthenia Gravis, Proc. Roy. Soc. Med. **28:** 759 (April) 1935. Everts, W. H.: The Treatment of Myasthenia Gravis by the Oral Administration of Prostigmine, Bull. Neurol. Inst. New York **4:** 523 (Dec.) 1935.

11. Perlow, Samuel: Vasodilating Action of Prostigmine, J. Pharmacol. & Exper. Therap. **66:** 66 (May) 1939.

tion of the cutaneous temperature lasted from two to six hours. The degree of elevation depended on the degree of vasospasm present.

The present report deals with the use of prostigmine in the treatment of some of the peripheral circulatory disturbances. We have used this drug clinically in thirty-one cases: eleven cases of thrombo-angiitis obliterans, four of arteriosclerosis, nine of Raynaud's syndrome, five of acrocyanosis and two of acute vascular occlusion. At first each patient was given a subcutaneous injection of 0.5 mg. of prostigmine and the temperature of the involved extremity was noted to determine the degree of vasodilatation produced. Then the patients were given 7.5 mg. of prostigmine orally three times daily at six hour intervals for a week without any other treatment. The effect of this medication was noted. If no improvement occurred, the dose was increased to 15 mg. of prostigmine three times daily. When and if improvement did result, such as increase in the walking distance or an elevation of the digital cutaneous temperature, a placebo tablet of the same size and shape as the prostigmine was substituted to rule out the possibility that the result was due to the psychic element of taking medication. The results in our cases are shown in the accompanying table.

RESULTS

Of the eleven cases of thrombo-angiitis obliterans there was an improvement in the walking distance and an elevation of the digital skin temperature in seven and no improvement in four. The latter were cases of long standing organic occlusion with apparently no element of vasospasm. One of the patients who improved with prostigmine had a rise of 6 degrees C. in the cutaneous temperature, and the walking distance was increased from half a block to a distance of one mile. Another patient who improved was a woman with thrombo-angiitis obliterans of three extremities; ulcers of the fingers of long duration healed in four weeks with prostigmine therapy alone.

There was slight improvement in only one of the four cases of arteriosclerosis. The degree of vasospasm present was very slight in all of these cases, as determined by peripheral nerve anesthetization.

Of the nine cases of Raynaud's syndrome there was a marked improvement, i. e. complete disappearance of the attacks of vasospasm, in five cases with mild attacks and slight improvement in one case with moderately severe attacks. There was no improvement in three severe cases of Raynaud's syndrome. In one of the latter cases attacks of vasospasm continued even when the dose of the prostigmine was increased to 30 mg. four times daily. In one of the cases in which improvement occurred a coexisting sclerodactylia improved as the attacks of vasospasm disappeared. In another case mild symptoms of vasospasm recurred after a previous sympathetic ganglionectomy, and these symptoms were relieved by prostigmine. An interesting observation in another case was the disappearance of coexisting attacks of angina pectoris when prostigmine was administered. These attacks recurred along with the vasospasm of the extremities when a placebo was substituted. However, in one of the severe cases of Raynaud's syndrome with coexisting angina pectoris neither the angina pectoris nor the vasospasm of the extremities improved with prostigmine therapy. This problem of angina pectoris is being studied further.

Of the five cases of acrocyanosis there was marked improvement with return of the color of the hands to normal in one case. In three other cases, which were severe, prostigmine caused the cutaneous temperature to rise to normal but the reddish cyanotic color of the hands remained. The fifth case showed no improvement at all with the doses used.

In addition to the foregoing cases prostigmine was administered subcutaneously in two cases of acute arterial occlusion. The first patient, with embolic occlusion of the left iliac artery, was seen four days after the onset. The extremity was cold and cyanotic up to the midthigh even though papavarine had been administered throughout the illness. Within four hours after prostigmine was given the cold blue area had receded to below the knee. Unfortunately this patient died a day later from a coexisting heart disease, so the observations were necessarily incomplete. In the other case there was an acute thrombotic occlusion of both femoral arteries. The extremities were blue, cold and anesthetic to the knees. Improvement was noted within two hours after prostigmine was administered, and the improvement continued with prostigmine therapy until, by the end of one week, both feet were warm and of normal appearance and all that remained was a small area of cutaneous gangrene at the ends of the left second, third and fourth toes.

In the cases of organic vascular occlusion that improved with prostigmine therapy the resultant improvement in circulation remained when, after several months, prostigmine was discontinued. Apparently a collateral circulation developed when the element of spasm was removed. That this was not coincidental is evidenced by the failure to bring about improvement in those cases by other therapeutic measures before prostigmine was given and by the fact that there was a return of the symptoms when prostigmine was stopped early in the course of treatment. In the cases with primary vasomotor disturbances such as Raynaud's syndrome and acrocyanosis the improvement lasted only as long as prostigmine was administered.

We found that most of our patients were able to tolerate doses of from 45 to 60 mg. of prostigmine orally without having abdominal cramps. In the few cases in which abdominal cramps and diarrhea did develop from the use of the drug a tablet of $\frac{1}{100}$ grain (0.00065 Gm.) atropine placed under the tongue gave relief very quickly. As in the previous report,[11] we found that subcutaneous injections of 0.5 mg. of prostigmine produce a greater and more prolonged temperature elevation than occurs when the drug is administered orally.

CONCLUSION

The results in thirty-one cases of peripheral circulatory disturbance indicate that prostigmine is an excellent vasodilator and as such is a useful adjunct in the treatment of peripheral circulatory disturbances in which vasospasm is a factor. The mechanism of its action, as has been shown by others, is neutralization of choline-esterase, thus permiting the cholinergic substances normally present to act at the parasympathetic nerve endings.

There is an improvement in the collateral circulation in the cases with occlusive vascular disease when the element of vasospasm is relieved. In the cases with mild primary vasomotor disturbances in the extremities, relief from the symptoms continues as long as prostigmine is administered and recurs when it is stopped.

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PARALYSIS OF THE SERRATUS MAGNUS MUSCLE

CAUSED BY LESIONS OF THE LONG THORACIC NERVE

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Unusual winging of the scapula is a deformity which is fairly well recognized as secondary in some instances to paralysis of the serratus magnus muscle. Description of this syndrome was first made by Velpeau [1] in 1825. Sir Charles Bell [2] in 1827 described the nerve supply of the serratus magnus muscle. The condition has been described by various writers since the time of Velpeau and Bell, notably by Marchessaux [3] in 1840 and by Duchenne [1] in 1867. Several methods of treatment have been suggested from time to time and several operative procedures have been offered. In order to estimate the relative incidence of this condition and

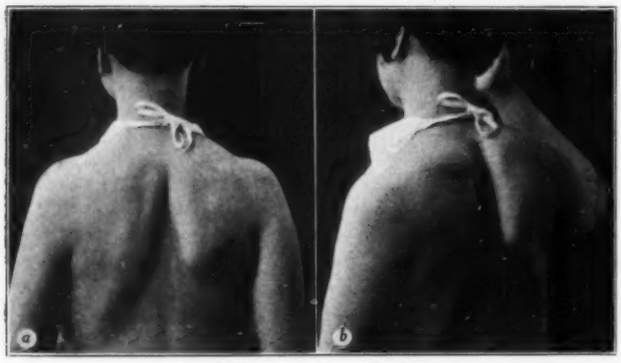

Fig. 1.—Paralysis of the serratus magnus muscle resulting from a miscarriage and the patient's habit of raising herself from bed by her right arm: *a*, winging of the right scapula with the arms pendent; *b*, oblique view of the right scapula. Picture taken on June 1, 1927.

to aid in our ability to prognosticate the end result in an instance of the disease newly seen, this study was undertaken.

The function of the serratus magnus muscle is mainly to aid in fixing the scapula to the thorax when the arm is elevated, particularly anteriorly, and also to rotate the scapula in abduction and during forward elevation of the arm at the shoulder. Stookey has proposed a more elaborate interpretation of the functioning of the serratus magnus muscle than is set forth in the foregoing sentence. He wrote that during elevation of the arm there are three cycles: the first is carried out by the deltoid and supraspinatus muscles, the second by the serratus magnus, trapezius, rhomboideus and levator scapulae muscles, and the third by the action of both the deltoid and supraspinatus muscles.

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Abridgment of thesis submitted by Dr. Overpeck to the faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of M.S. in Orthopedic Surgery.

1. Quoted by Souques, A., and Castaigne, J.: Contribution à l'étude de la paralysie isolée du muscle grand dentelé, Nouv. iconog. de la Salpêtrière **12**: 177-196 (May-June) 1899.

2. Bell, John, and Bell, Charles: The Anatomy and Physiology of the Human Body, fifth American edition, New York, Collins & Co., 1827, vol. 1.

3. Marchessaux, L.: Observation de paralysie du muscle grand dentelé, avec réflexions sur cette affection, Arch. gén. de méd. **52**: 313-318 (March) 1840.

SYMPTOMATOLOGY

The most prominent symptom of isolated paralysis of the long thoracic nerve and the serratus magnus muscle is pain. Pain usually extends along the base of the neck and downward over the scapular and deltoid regions on the affected side. Frequently there is a painful region in the axilla, especially over the mid-axillary line and downward as far as the sixth or seventh rib. There may be extension of the pain upward to the back of the head or downward over the arm and into the forearm and hand. Following injury to the muscle there is often severe pain at the site of the trauma, which may be under the scapula, deep in the axilla or over the digitations of the muscle in the anterior portion of the wall of the thorax. The severity of the pain aids the physician in making a differential diagnosis, because trauma to the muscle produces a more severe type of pain than that seen with involvement of the nerve only.

The second most common symptom is the patient's fatigue on elevating the arm or the inability fully to elevate the arm. The weakness may arise unnoticed by the patient. A third symptom is the abnormal prominence of the scapula, a sign more frequently noticed by others than by the patient himself. The time of onset of the pain is usually immediately after acute trauma but is variable in the case of other types of trauma and infection. Weakness of abduction does not begin at the time of the onset of pain, except when acute traumatic lesions are present.

On examination of the patient, the principal clinical observations are weakness of the pushing power of the affected shoulder and weakness of the abducting power of the arm above the horizontal plane. Winging of the scapula is always present when the arm is fully abducted or is elevated anteriorly. Some winging also occurs in many instances in which the arm is pendent.

Isolated paralysis of the long thoracic nerve or of the serratus magnus muscle occurs rarely. Remak [1] reported three cases in a series of 12,000 neurologic examinations. This produced a percentage of 0.025 in such cases. At the Mayo Clinic there have been twenty-eight cases in which diagnosis of the condition was made, resulting in a percentile incidence of about 0.0026. There were nineteen men and nine women in the series. There was involvement of the upper right extremity in twenty-two cases, of the upper left extremity in five cases, and bilateral involvement in one case. Twenty-two patients were between the ages of 20 and 50 years. Nineteen of the patients worked at some form of heavy labor.

CAUSATION

Trauma was the chief causative agent in the present series, twenty-three instances of the condition, or 82 per cent of the total number of cases, being the result of some type of trauma. The various types of trauma were classified as (1) the acute type, (2) the recurrent irritative type and (3) the contributive type of trauma.

There were fifteen of the twenty-eight cases, or 53 per cent, in type 1, the acute type of trauma. This included one case of paralysis of the long thoracic nerve subsequent to traction on the patient's hands and arms during birth. One instance of the condition followed operative removal of diseased cervical lymph glands in which the long thoracic nerve was directly injured. Another instance followed an operation on the face and was related to trauma to the shoulder girdle while the patient reclined on an unpadded table. One instance occurred after the patient made a vigorous swing at a

punching bag and missed it. A horse kicked one patient in the axilla, injuring the long thoracic nerve and producing the lesion. An energetic pull on the hand clutch of a mechanical device by a patient brought about paralysis of the long thoracic nerve. A golfer missed the golf ball on a lusty swing and the lesion developed therefrom. In addition to the cases cited, there were eight in which the condition resulted from falls on the shoulder girdle. It has been shown that the coracoid process may be forced against the underlying first or second rib and thus injure the intervening long thoracic nerve.

Five patients exhibited evidence of acute traumatic separation of a portion of the serratus magnus muscle, in addition to injury of the long thoracic nerve. The muscle may be pulled away from the scapula or from the digitations attached to the ribs. The question of injury to nerves or muscles in producing the clinical signs and symptoms in such cases as are being described is one that has never been settled completely. Unquestionably the majority if not all of the patients affected have an injury to a nerve or nerves. Actual tear through the muscle, or separation of the muscular attachment, should be fairly easily diagnosed at the time of the injury. However, when patients are seen later in their convalescence the differential diagnosis may be more difficult than it would have been at or near the time of injury. Five of our patients had diagnoses of separation or tear of the attachment of the muscle to the scapular border. None of these patients underwent surgical exploration, however, and there may be some doubt as to the presence of the muscular tear. Absolute diagnosis probably can be made only by open exploratory operation.

Under type 2, the recurrent irritative type of trauma, there were classified seven cases, which comprised 25 per cent of the total number of cases. In one instance the lesion resulted after the patient, a carpenter, had carried boards on his shoulder over a period of three years. Pressure on the shoulder, combined with angulation of the patient's head to the opposite side, has been cited as a causative factor by several writers.

Trauma to the side of the neck in the region of the scalenus medius muscle has been observed to have been

Fig. 2.—*a*, same patient as in figure 1, demonstrating increase in winging of the right scapula on abduction of the arm (June 1, 1927); *b*, same patient Nov. 17, 1938, in whose right scapula no winging can be detected with arms pendent.

increased when the person who had been carrying an object on one shoulder unloaded the object from the shoulder with a powerful shrug. One of the patients in the present series was afflicted by the lesion following the use of crutches in conjunction with a fractured leg. Such an instance should emphasize the importance of patients' maintaining most of their weight on the handle of the crutch and to avoid allowing that portion of the crutch which fits into the axilla to press on the lateral thoracic wall over the course of the long thoracic nerve. Another instance of the condition resulted from a cast which pressed persistently into the axilla. Two instances followed a patient's postural habit of sleeping on the outstretched arm.

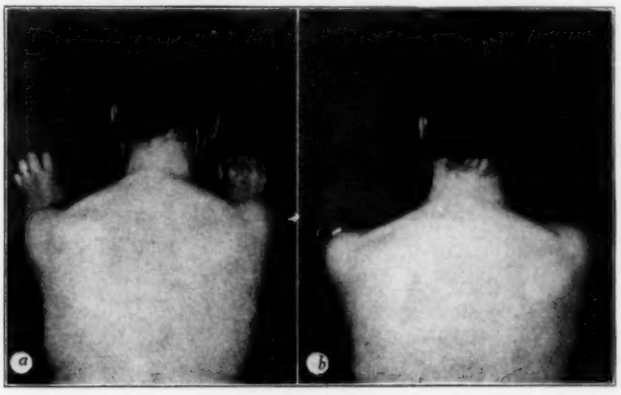

Fig. 3.—*a*, same patient, demonstrating absence of winging of the right scapula even when the patient pushes against wall; *b*, same patient, absence of winging of the right scapula with arms abducted. Pictures taken Nov. 17, 1938.

Potts [4] in 1928 indicated that injury to the long thoracic nerve occurred in conjunction with patients' sleeping on the abducted arm and rolling about during sleep, so that the nerve fibers to the inferior digitations of the serratus magnus muscle were stretched.

One patient in our series suffered the lesion following a miscarriage. She frequently lifted herself from the bed on her right arm and thereby stretched the long thoracic nerve. The final case in this group concerned trauma associated with husking corn.

Skillern [5] in 1913 cited a similar case in which the trauma supposedly resulted from the fact that a machinist had to reach fully forward more than 800 times in the course of each daily shift of work.

One case was classified under type 3, the combined type of trauma, the percentage of this type therefore being 3.5 of the total number of our cases. In the history of the patient concerned there was a definite relationship of the trauma to strenuous work and exposure to bad weather. Foucar [6] in 1933 described a case in which he believed the condition resulted from a combination of cervical adenitis and tennis playing.

Another causative agent was infectious conditions. In the present series, one instance of the paralysis developed subsequent to influenza and one instance followed brachial neuritis. These two cases comprised 7 per cent of the total. There were three cases, or 11 per cent, of unknown causation.

TREATMENT

Treatment may be divided into two types: conservative and operative. Various types of conservative measures may be tried, such as supporting splints and bandages and physical therapeutic measures such as heat, massage and galvanic stimulation. The accompanying illustrations show the

4. Potts, C. S.: Isolated Paralysis of the Serratus Magnus; Report of a Case, Arch. Neurol. & Psychiat. **20**: 184-186 (July) 1928.
5. Skillern, P. G., Jr.: Serratus Magnus Palsy with Proposal of a New Operation for Intractable Cases, Ann. Surg. **57**: 909-915 (June) 1913.
6. Foucar, H. O.: The "Clover Leaf" Sling in Paralysis of the Serratus Magnus, Brit. M. J. **2**: 865-866 (Nov. 11) 1933.

condition of one patient of our series both at examination in 1927 and after a course of physical therapy. Many mechanical appliances have been devised, but none are adequate to substitute for the function of the serratus magnus muscle. Some type of mechanical support should be tried in order to relieve the patient of pain, if possible, and to relax tension on the serratus magnus muscle. Persistent efforts in conservative measures may give the patient complete recovery, as is demonstrated by the follow-up observations on our own group of patients. Reassurance on this basis may do much to aid the patient's recovery. Certainly, avoidance of heavy muscular effort involving the affected muscle should be advised.

A review of the literature revealed that there were the following types of surgical treatment: (1) fixation of the scapula to the underlying ribs, (2) substitution of an adjacent subscapular nerve for the long thoracic nerve, and (3) transplants of the various muscles of the shoulder girdle.

Only a temporary improvement followed fixation of the scapula with wire to the underlying ribs. The same resulting support would be obtained if an abduction arm brace should be used.

Skillern [5] in 1913 reported a plan for substituting one of the three adjacent subscapular nerves for the long thoracic nerve, but no cases in which this was done have been reported. Samter [7] in 1930 reported an excellent result of twenty-two years' duration in which he transplanted a portion of the pectoralis major muscle from the humerus to the serratus magnus muscle. Hass [8] in 1931 reported a good result, after fifteen years, accruing from transplantation of the teres major muscle from the humerus to the digitations of the serratus magnus muscle. Many other similar attempts at transplantation of muscle have not been successful. The results of surgical treatment have not been considered, on the whole, worth the operative risk, work and expense.

In the present series, only conservative treatment was used; it consisted of physical therapy and in addition, in some instances, elevation of the arm of the patient for a period of several weeks.

A follow-up of fifteen patients indicated good results in eleven instances. There was complete recovery for seven of these eleven patients, whereas four patients enjoyed recovery of strength but had persistent winging of the scapula. Three patients whose conditions were caused by trauma did not recover.

SUMMARY AND CONCLUSIONS

Paralysis of the long thoracic nerve and the serratus magnus muscle is a rare lesion. It occurs most frequently among men who do heavy labor and who are between the ages of 20 and 50 years. Trauma is the chief causative factor. Weakness of the power of complete abduction and winging of the scapula are salient physical observations. Physical therapy and support of the extremity are the most universally successful methods of treatment. The prognosis for restoration of function is good in the majority of instances of the condition.

7. Samter: Sur le traitement opératoire de la paralysie du grand dentelé, abstr. J. de chir. **1**: 299 (Feb.) 1930.

8. Hass, Julius: Muskelplastik bei Serratuslähmung (Ersatz des gelähmten Musculus serratus anterior durch den Musculus teres major) Ztschr. f. orthop. Chir. **55**: 617-622, 1931.

Clinical Notes, Suggestions and New Instruments

FRACTURE OF THE POSTERIOR ARCH OF THE ATLAS

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Statistics show that the "broken neck," as spoken of by the public, is not necessarily or usually fatal.[1] Fracture of the bodies of the lower cervical vertebrae, as well as of the atlas, is rarely followed by death. This is not true of fracture of the odontoid process, which is the mechanism of death by hanging. In fractures of the atlas a 13.7 per cent mortality has been reported since 1900.[2] The strong transverse ligament that crosses the odontoid posteriorly serves to preserve the normal anatomic relation between the atlas and the surrounding structures, even in fracture of each posterior arch.

The rarity of fracture of the atlas is attested by the fact that only ninety-three cases had been reported to 1938.[1a] Situated at the base of the skull and surrounded by strong bundles of muscle, the atlas is rarely fractured as the result of a direct trauma. The usual mechanism is the pressure of the occiput on a rigid cervical spine with the muscles of the neck relaxed, conditions which usually obtain in automobile and railroad accidents. The type of accident that resulted in the fracture

Fig. 1 (case 1).—Note the compression of the left lateral mass and the shift of the atlas to the right.

described in case 1 is most unusual, but the factors just mentioned were present. The usual fracture site is in the posterior arch (unilateral or bilateral) near the lateral masses where the groove for the vertebral artery narrows the bony structure. Fracture of the anterior arch, the lateral masses and the transverse processes are quite unusual.

The history, the physical condition of stiffness and painful restricted movement of the neck, and the roentgenograms make the diagnosis. Plaut prefers lateral roentgenograms.[1b] We have secured additional information by oblique views taken with the patient supine and the head turned if possible to a 45 degree angle, first to one side and then to the other. The head is flexed to avoid overlapping of the occiput. The Bucky technic is used. This technic is possible only in the period of healing when plaster fixation has been removed. It is not advised in the acute stage. A second method of securing oblique views is to place the patient in the usual lateral skull position and center the tube over the atlas. The posterior arches are well visualized by this technic. To secure anteroposterior views the open mouth technic is employed. Ottonello's

1. Plaut, H. F.: (*a*) Fracture of Atlas in Automobile Accidents, J. A. M. A. **110**: 1892-1894 (June 4) 1938; (*b*) Radiology **29**: 227-231 (Aug.) 1937.

2. Jefferson, G.: Remarks on Fractures on the First Cervical Vertebra, Brit. M. J. **2**: 153 (July 30) 1927. Plaut.[1b]

method has been used and found satisfactory.[3] To secure views of the anterior arch, a dental film may be placed in back of the oral cavity and the x-rays projected from the back of the neck. With a patient in a cast, only lateral views are satisfactory. The employment of a castex bandage, which is radiolucent, is sometimes preferable.

From the roentgenologic standpoint, congenital bony defects must be differentiated from fractures. These defects are usually found near the posterior tubercle. When they are of considerable width (10 mm.) they must not be confused with fractures with displacement. Follow-up roentgenograms that show evidence of callus are important in differential diagnosis of fracture from congenital defect. At times, fractures of the atlas do not unite and end in pseudo-arthrosis. The question is not simple and requires all the skill of an expert radiologist.[4]

Treatment of fractures of the atlas, whether of the lateral mass or of the anterior or posterior arch, is the same as treatment of fracture of the cervical spine elsewhere. The patient's neck is hyperextended in bed by traction and a plaster jacket of the Calot type applied when the acute stage is over. This jacket is worn until healing occurs. At this time the neck should be supported by a brace and physical therapy is given. The total duration of treatment is as for any cervical spine injury, about seven to twelve months.

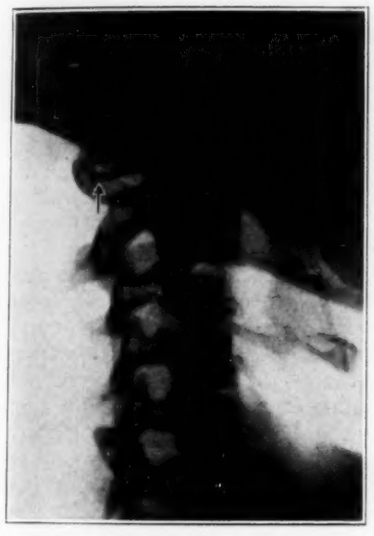

Fig. 2 (case 1).—Note the complete longitudinal fracture of the left posterior arch of the atlas near the posterior tubercle.

Fig. 3 (case 2).—Note the complete longitudinal fracture of the left posterior arch of the atlas and compression fractures of the bodies of the third and fifth cervical vertebrae.

Fig. 4 (case 2).—Left oblique view showing the fracture of the left posterior arch of the atlas.

REPORT OF CASES

CASE 1.—N. R., a man aged 22, sustained a fracture of the first cervical vertebra in a gymnastic accident at school when he landed squarely on his head in doing a turn on the parallel bars. He was admitted to the Hospital for Joint Diseases, March 29, 1938. X-ray examination (figs. 1 and 2) showed a compression fracture of the left lateral mass and a complete longitudinal fracture of the left posterior arch of the atlas near the posterior tubercle. There was a shift of the atlas to the right. He was placed in head and neck traction for two weeks and a Calot jacket was then applied. There were no other significant signs besides local tenderness and restriction of motion.

On June 10 the cast was removed and a castex bandage applied, which was later converted into a brace. On September 19 flexion of the neck was slightly limited and extension was complete. Lateral motion was limited and rotation to the right and left did not exceed 10 degrees. The neck was not tender and he discontinued use of the castex bandage. Examination Nov. 1, 1938, and April 1, 1939, showed flexion and extension to be complete. Passive rotation was almost complete, but active rotation was about two thirds normal. Lateral motions were two thirds normal, the upper cervical spine moving as a unit rather than in its individual parts. On Sept. 18, 1939, the patient had no complaints referable to the neck. Rotation to the right was slightly limited and there was still some limitation of the lateral motions. The neck moved as a rod, as noted previously. Bony union at the fractured posterior arch was not present June 20, 1938, but was present September 9. On Jan. 1, 1939, sclerotic changes were noted about the left lateral mass and there was narrowing of the intervertebral space between it and the body of the second cervical segment. The fracture of the left posterior arch was healed by bony union.

CASE 2.—M. C., a Negro aged 52, on Oct. 9, 1937, fell from a platform a distance of about 30 feet to the main floor of a tunnel and was struck over the neck by a street car rail. He injured his neck, skull and right scapula. The right lung was pierced. He was unconscious and taken to a hospital. It was found that he had sustained a fracture, with no displacement of the fourth and fifth ribs on the right side, 1 or 1½ inches from the vertebral articulations. A pneumothorax on the right side with partial collapse of the right lung developed. A fracture of the left posterior arch of the first cervical vertebra was seen on roentgenograms. The right scapula showed comminution. He remained at the hospital until November 1.

Examination December 21 showed numerous disabilities due to his fractured shoulder and ribs which are irrelevant here. He complained of sharp pain in the neck, especially at night. This pain was usually dull and radiated to both shoulders. Turning the head to the left increased the pain. He believed that the street car rail had not hit his head directly. Lateral motions of the neck were limited. Flexion and extension of the neck as well as rotation were fairly good. Tenderness was present over the second and over the fifth spinous processes. The cervical spine in the region of the second and third cervical vertebrae was kyphotic. The patient was admitted soon after this to the Hospital for Joint Diseases. The head and neck were kept in traction on a convex frame. The shoulder was also maintained in traction in abduction. The neck was thereafter immobilized in a Calot jacket. A brace was worn from March 7 to July 7, 1938.

On Sept. 2, 1938, all motions of the neck were complete. There were no tender points. He occasionally had slight pains in the upper part of the right trapezius muscle. The neck now moved well in its individual parts, where previously it had moved rather as a unit.

On Aug. 23, 1939, he complained that he had a dull ache of the neck at times, usually in rainy weather, and a fairly

3. Jacobs, L. G.: Second Cervical Vertebra by Ottonello's Method, Radiology **31**: 412 (Oct.) 1938.
4. Lawrence, W. S., and Anderson, W. D.: Rare Developmental Anomalies of the Atlas, Radiology **28**: 55-57 (Jan.) 1937. Plaut.[1b]

constant dull ache of the right shoulder. Physical examination of the neck was as before.

Roentgenograms taken Dec. 2, 1937 (fig. 3), disclosed a complete longitudinal fracture of the left posterior arch of the atlas together with a compression fracture of the bodies of the third and fifth cervical vertebrae. There was slight

Fig. 5 (case 2).—Left oblique view showing bony bridging at the fracture site in the left posterior arch of the atlas. Compare with figure 4.

posterior displacement of the body of the fifth cervical vertebra with marked narrowing of the intervertebral space between the fifth and the sixth cervical vertebra. Oblique views taken on December 27 showed similar conditions (fig. 4).

Roentgenograms taken March 7, 1938, demonstrated bony bridging of the fractured left posterior arch of the atlas. This was confirmed by a roentgenogram taken in the left oblique view on April 1 (fig. 5).

Fig. 6 (case 2).—Lateral view showing bony bridging at the fracture site in the left posterior arch of the atlas. Compare with figure 3.

Roentgenograms taken November 8 showed a compression fracture of the third and the fifth cervical vertebra associated with some wedging of these segments. Hypertrophic marginal changes were present on the inferior aspect of the third, fourth and fifth cervical vertebrae. The fracture of the left posterior arch showed bony union. There was a slight loss in the normal cervical curve.

On Aug. 24, 1939, roentgenograms of the cervical spine showed restoration of its curve (fig. 6). Osteo-arthritic changes of the fourth and fifth cervical vertebrae were noted. There was still diminution of the height of the third and fifth but the fracture had healed well. There was some narrowing of the intervertebral spaces between the fourth and fifth and the fifth and sixth cervical vertebrae. The fracture of the atlas was well healed.

SUMMARY

Of two cases of fracture of the posterior arch of the atlas, one was associated with a crushing fracture of a lateral mass and the second with a fracture of other bodies of the cervical spine, together with fractures of other skeletal structures.

It would seem that fracture of the posterior arch of the atlas is not an independent fracture but is associated with fracture of the cervical spine at other points.

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Special Articles

THE PHARMACOPEIA AND THE PHYSICIAN

THE USE OF DRUGS IN ASTHMA

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This is one of the second series of articles written by eminent authorities for the purpose of extending information concerning the official medicines. The twenty-four articles in this series have been planned and developed through the cooperation of the U. S. Pharmacopeial Committee of Revision and THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.—ED.

As knowledge of asthma increases, it becomes more and more clear that the wheezy breathing is merely a symptom. The important part of the treatment must be to find and remove the cause. What good are drugs if the patient is going to lose all his symptoms within a few hours after moving to the clean environment of the hospital or even to another house, or if his asthma will clear as soon as the cat or the dog or perhaps the kapok mattress is eliminated? However, such a simple happy outcome occurs only in the simple "textbook" cases, which comprise only a fraction of the total number. The great number of patients must have drugs of some sort for relief of real distress, and they may need other drugs for the treatment of the underlying causes of the asthma.

DRUGS FOR RELIEF

Drugs for relief are widely used and will be discussed in the order of their efficacy. When the attack of asthma is mild, simple measures will relieve it. The burning of "asthma powder," best made from equal parts of dried powdered stramonium leaves and potassium nitrate (saltpetre), gives off a smoke which, when inhaled, is often quite effective. Cigarets prepared from these materials are on the market in several varieties. Objections include the danger of fire and the smell of the smoke, which some find disagreeable.

Ephedrine by mouth is useful. Its action is like that of epinephrine to stimulate the sympathetic nerves and so to overcome bronchoconstriction, to reduce vasodilatation and consequently to modify the overactivity of the mucous glands in the bronchial mucosa. It is given by mouth in the form of its salts, the sulfate or the hydrochloride, and in each form the dose varies from 0.025 to 0.050 Gm. (three eighths to three fourths grain). Ephedrine can be prescribed in capsules, in pills or in a fluid mixture, either a watery syrup or a dilute alcohol being used; a useful formula is given in the accompanying prescription.

The action of ephedrine is slow and so the dose is given best after the evening meal and not as late as

bedtime. Small children and some adults will be kept awake by ephedrine, and it is on account of this exciting effect that combinations of various barbiturates with ephedrine have been put forward by the pharmaceutic houses. These combinations are often effective. For older men ephedrine should be prescribed cautiously, because it may irritate the prostate and bladder and cause dysuria.

Propadrine hydrochloride is derived from a base resembling ephedrine. Black [1] finds it useful in mild attacks, though less effective than ephedrine. The dose is 0.025 Gm. and is to be given by mouth in capsule form every two to four hours, as indicated.

Drugs given by inhalation in the form of a spray are often very useful for the relief of asthma and many patients depend on them. Their efficacy depends on the ability of the patient to inhale the spray and so to bring the drug into direct contact with the bronchial mucosa. The patient must be taught, therefore, to squeeze the bulb of the atomizer at the moment of inspiration. The good effects of inhalation of a drug finely dispersed in air throw an interesting light on the mechanism of asthma as well as on the method by which inhaled substances are absorbed. Several drugs are used in sprays for the relief of the asthmatic paroxysms. In the order of their importance they are as follows:

Ephedrine Sulfate in Aromatic Elixir

	Gm. or Cc.
℞ Ephedrine sulfate	0.75
Elixir aromatic to make	120.00

Mix and label: Teaspoonful in water after supper; repeat once during the night if necessary.

Epinephrine 1:100 is most effective. It is a special preparation made ten times as strong as the ordinary epinephrine (adrenalin) 1:1,000 dilution. It was first proposed by Graeser and Rowe [2] in 1935 and should be used with the special type of glass nebulizer which is made for the purpose and is ordinarily dispensed with it as an "outfit." One must emphasize that this is "strong stuff" to be used only in the form of a spray, for within the year there have appeared several reports of serious reactions and at least one death when this strong material was used for hypodermic medication in place of the usual 1:1,000 dilution of epinephrine. The epinephrine 1:100 spray should bring relief within a few minutes even if the attack of asthma is quite severe, but the patient must know that two or three squeezes properly inhaled are as good as more and that this application will take a little time to act. If it does not act, then the patient had better take the epinephrine 1:1,000 by needle. If it does act, the atomizer can be used again in an hour or two, but the patient should understand that too much of the epinephrine 1:100 spray may injure the bronchial mucous membrane. There are a few fortunate patients who find that the "ordinary" 1:1,000 epinephrine can be used as a spray with successful relief of their attacks, but this is not common. Ephedrine sprays are not so effective as epinephrine, and neither are the other drugs related to ephedrine as useful as epinephrine. These, however, have another use in the local treatment of the nose and sinuses in asthma, as will be discussed presently.

Epinephrine 1:1,000 by hypodermic injection is the treatment of choice when asthma from any cause becomes severe and no longer yields to simple remedies. Epinephrine is effective by mouth only in rare instances. For hypodermic use the usual preparation is the 1:1,000 dilution of epinephrine hydrochloride. The dose is always important, for in most cases too much is given. Very often a dose of 0.25 cc. (4 minims) of the 1:1,000 dilution will relieve the asthma quite as well as a larger quantity, and when this dosage is employed disagreeable by-effects such as pallor, tachycardia and sweating are avoided. Epinephrine can be injected often—every hour or every half hour if necessary. This means that in severe cases relatively enormous total quantities are used. Patients who use as much as 30 cc. (1 ounce) of the 1:1,000 dilution in a week are not uncommon, and Waldbott [3] describes one case in which 30 cc. a day was taken.

Can epinephrine do any harm if used continuously over long periods of time? So far no evidence has been found to indicate damage to the heart, liver, kidneys or any other organ, and the literature contains several reports of long standing asthma in which large amounts of epinephrine were taken daily for four or five years. In one such case Rackemann and Theiler [4] figured that the quantity consumed in three years was 280 bottles of 30 cc. each.

Epinephrine in oil ("slow epinephrine") has been devised by Keeney and his co-workers.[5] The powdered epinephrine base is suspended in sterile peanut oil in such proportions that 1 cc. of the oil contains 2 mg. of epinephrine. Doses of from 0.5 to 1.5 cc. are injected intramuscularly, usually in the late afternoon, and patients with asthma or with hay fever will often be relieved for as long as sixteen hours. For some patients the method is very satisfactory, but in others the doses cause local reactions (redness and swelling), which may be troublesome.

"STATUS ASTHMATICUS"

"Status asthmaticus" describes the condition in which epinephrine is no longer effective. Such a condition is serious. The suffering is severe and, although deaths from asthma alone are not common, death may occur from suffocation produced by the formation of tough sticky plugs of mucus in the lumen of the larger as well as of the smaller bronchi. The treatment has been discussed by Waldbott.[3] The first principle is to avoid those antigens (dusts, foods and particularly drugs) to which the patient may be sensitive, even though cutaneous tests do not always give positive results. The elimination of extrinsic factors such as the cat or dog or the dusty pillow and mattress should be a routine procedure, as also the elimination of suspicious foods and drugs. Transference to the clean environment of a hospital, which eliminates automatically many offending substances, has solved many a problem of sleepless nights and brought prompt relief to the patient and to every one concerned for him, including the physician. Obviously, these patients need rest and sleep and of course one is tempted to use sedatives of all sorts, but there are serious objections to the indiscriminate use of drugs in this condition.

DRUG ALLERGY

Drug allergy is of great practical importance, more so than is usually appreciated.

1. Black, J. H.: The Control of Allergic Manifestations by Phenyl-Propanol-Amine (Propadrine) Hydrochloride, Journal-Lancet **57**: 101 (March) 1937.
2. Graeser, J. B., and Rowe, A. H.: Inhalation of Epinephrine Hydrochloride for Relief of Asthmatic Symptoms, J. Allergy **6**: 415 (July) 1935.
3. Waldbott, G. L.: Emergency Treatment in Asthma (Asthmatic Crisis), J. A. M. A. **110**: 1423 (April 30) 1938.
4. Rackemann, F. M., and Theiler, Hans: Asthma of Maximum Severity but with Great Improvement After Three Years, J. Allergy **7**: 523 (July) 1936.
5. Keeney, E. L.: A Slowly Absorbed Epinephrine Preparation: Preliminary Report, Bull. Johns Hopkins Hosp. **62**: 227 (March) 1938.

Acetylsalicylic acid (aspirin) is taken so freely by the American people that the development of hypersensitiveness to it is not uncommon. Once I almost killed a man with 5 grains (0.3 Gm.) of acetylsalicylic acid. Sensitiveness to this drug often occurs precisely in those cases in which asthma is severe. It almost defines a special group of difficult cases.

Morphine and its relatives may also cause trouble, and in more than one case the status has been maintained rather than improved by morphine. I recall a woman aged 45 in status asthmaticus for whom bronchoscopy was advised, and as a preparation one fourth grain (0.016 Gm.) of morphine sulfate was injected subcutaneously. After the operation her condition was desperate for a few hours and she was in the hospital for four weeks. On another occasion bronchoscopy was performed again for severe asthma, and this time without drugs of any kind. Relief was prompt and she was in the hospital only five days.

The barbital group of drugs may produce hypersensitiveness, but reactions in the form of increased asthma are not common. For some reason sensitiveness to the barbiturates results more often in cutaneous lesions—urticaria, erythema and eczema—or occasionally in gastrointestinal symptoms.

This emphasis on the bad effects of drugs in asthma is necessary; I have seen more than one patient greatly improve when drugs were withheld. On the other hand, it is obvious that many patients with severe asthma have been much benefited by the careful use of acetylsalicylic acid, morphine or barbital compounds. If the physician will appreciate the danger and will ask for the patient's previous experiences with drugs and then will abide by them, he will do good and not harm.

TREATMENT

Symptomatic treatment of severe cases is not easy, particularly if the physician hesitates to use those very drugs which first suggest themselves to him. Here is a man, gasping for breath, sometimes a little cyanotic with rapid pulse, sweating, and exhausted by the constant, never ending effort to breathe. He dares not eat or drink and is anxious and apprehensive. What can be done? In my experience the giving of water, salt and sugar quickly is the next step after the injection of epinephrine. If the patient can drink a quart or so of liquid, hot or cold, in the form of tea, soup, lemonade or even plain water, his condition will improve, but, if he cannot take such quantities by mouth, fluid must be given by vein. In severe cases of asthma, the heart and kidneys are usually sound and there is no objection to the intravenous infusion of fluid. A liter or two of physiologic solution of sodium chloride or 5 or 10 per cent dextrose may give great relief, especially if from 1 to 2 cc. of epinephrine from ampules of the 1:1,000 solution is added to the infusion flask and mixed thoroughly with the contents. Any solution for intravenous use should be made carefully and with water freshly distilled just before use, unless the water has been specially preserved in sealed bottles blown from a special kind of glass. The injection should be given slowly, so that at least one hour is taken for each liter to run in. Whether the addition of dextrose accomplishes anything more than to provide a little food is doubtful, and consequently there is little real choice between a 5 and a 10 per cent solution of dextrose. The latter provides more food but is more irritating to the vein. Concentrated sugar solutions for intravenous injection have been advised: 50 per cent dextrose by Lepak [6] and 50 per cent sucrose by Gay [7]—the object being to withdraw fluid from the lungs and incidentally to provide calories, but I have had no experience with either.

Transfusion of whole blood from healthy, nonallergic donors has been recommended and deserves a much wider use in severe asthma. It might have an important immunologic effect. Cooke [8] has found experimentally that transfusion relieves hay fever. Presumably the donor should be fasting at the time of bleeding lest the patient be sensitive to some food or drug which the donor has recently taken; the type of blood should be compatible, of course.

What of drugs, especially if those which the physician first thinks of are precluded? Simple salts are safe. Chloral hydrate, paraldehyde and bromides are old fashioned sedatives but they also have simple chemical structures; they are useful and often are effective. So far they have not been found to give rise to hypersensitiveness, although a recent report by Kotz and others [9] describes an idiosyncrasy to paraldehyde as used in large doses in obstetrics. The dose of chloral hydrate is from 1 to 2 Gm. (15 to 30 grains) to be given by mouth at night in water or syrup. Chloral hydrate should never be used on a day that the patient has taken any alcohol. Paraldehyde is usually given by rectum in amounts of from 5 to 10 cc., also at bedtime, but paraldehyde can be given by mouth in doses of one half to a whole teaspoonful (2 to 4 cc.). In this way it takes effect almost at once and the patient seems almost to collapse into a drowsy stupor. The danger is that the respiratory center may be depressed at the same time, but the danger is not great.

More drastic treatment may be necessary. Aminophylline, a double salt or a mixture of theophylline with ethylenediamine, is a purine compound the action of which is to improve capillary blood flow. It has been used as a stimulant to both heart and kidneys in cardiorenal disease, and in 1937 Herrmann and Aynesworth [10] found it effective in asthma. I find it very useful for patients who no longer respond to epinephrine—who have become "epinephrine-fast." The dose often relieves the asthma for several hours and restores the normal reaction to epinephrine. The injection of one ampule intravenously on each of two or three evenings may bring the patient out of his status asthmaticus. The drug is given intravenously, the contents of an ampule containing 0.24 Gm. of aminophylline dissolved in 10 cc. of water being injected. The mode of action in asthma is not clear.

Theophylline alone is much less soluble, so that it cannot be used by vein, and by mouth it is not effective in asthma.

Ether in oil by rectum (30 cc., or 1 ounce, of ether to 60 cc., or 2 ounces, of olive oil) is less effective than aminophylline but it may be tried. It can be given on successive nights or even repeated on the same night without danger of depressing the respiratory center.

6. Lepak, J. A.: Relief of Acute Asthma by Intravenous Administration of Concentrated Glucose Solution: Report of Cases, Minnesota Med. **17**: 442 (Aug.) 1934.

7. Gay, L. N., in discussion before the Society for the Study of Asthma and Allied Conditions, New York, Dec. 11, 1937.

8. Cooke, R. A.; Loveless, Mary, and Stull, Arthur: Studies on Immunity in a Type of Human Allergy (Hay Fever): Serologic Response of Nonsensitive Individuals to Pollen Injections, J. Exper. Med. **66**: 689 (Dec.) 1937.

9. Kotz, Jacob; Roth, G. B., and Ryon, W. A.: Idiosyncrasy to Paraldehyde, J. A. M. A. **110**: 2145 (June 25) 1938.

10. Herrmann, George, and Aynesworth, M. B.: Successful Treatment of Persistent Extreme Dyspnea, "Status Asthmaticus": Use of Theophylline Ethylene Diamine (Aminophylline U. S. P.) Intravenously, J. Lab. & Clin. Med. **23**: 135 (Nov.) 1937.

But perhaps the asthma continues in spite of treatment with one or all of these drugs. Oxygen may be necessary, and for asthma an oxygen tent should be particularly effective. This is partly because the relief that comes from breathing an atmosphere containing 40 or even 100 per cent oxygen may be life saving, and partly because an oxygen tent provides almost perfect "air conditioning." Extrinsic factors are eliminated automatically, and if the asthma is caused by dust the tent should be particularly effective. The new B. L. B. mask designed by Boothby, Lovelace and Bulbulian [11] is a more economical and efficient device for giving oxygen. Like the tent, it has the function of excluding all dust factors. The mask has a number of air inlets which can be opened or closed, and with them one can adjust concentration of oxygen in the intake quite nicely. Helium has been used by Barach,[12] who points out that, whereas a mixture of oxygen and air (nitrogen) has a high molecular weight, the mixture of the same amount of oxygen with helium has a much lower weight and density and so is better able to pass through small orifices like the partially occluded bronchi. If, therefore, helium is available, it should be used, for it may be helpful.

BACKGROUND OF ASTHMA

The fundamental background of asthma often requires drugs in its treatment. In the simple "textbook" cases of extrinsic asthma, in which the fundamental cause is an allergic or atopic hypersensitiveness to a food or a dust, elimination is the important method of "fundamental" treatment and may be the only method required. Secondary infections occur and a chronic sinusitis or bronchitis makes a bad matter worse. Curiously the severity of the infection makes a difference, since a mild cold will always aggravate while a more severe and febrile disease will often lead to a rapid subsidence of the asthma.

Lesions of the nose and sinuses are so common in asthma that they may be regarded as a part of the process and not as a cause of it. This new regard explains why it is that the results of operation on the nose and sinuses are so often disappointing or at least have only a temporary good effect. Nevertheless the nasal lesions are often severe and require treatment and so sprays to the nose are used widely in the treatment of asthma and hay fever. They cause shrinkage of the nasal mucous membranes and so promote drainage of the sinuses. Too much shrinkage, however, may inhibit the recovery of the membrane itself. The problem has been discussed in a previous article in the first series of these papers on "Local Medication of the Upper Respiratory Tract" by Heatly.[13] The active ingredient in these sprays may be one of several drugs.

Ephedrine in the form of the alkaloid is miscible with oil, and a good spray is one containing from 1 to 2 per cent of ephedrine alkaloid in flavored liquid petrolatum. The ephedrine spray (nebula ephedrinae) of the National Formulary contains 1 per cent of ephedrine with methyl salicylate. The National Formulary also provides a compound ephedrine spray (nebula ephedrinae composita) containing 1 per cent ephedrine with camphor, menthol and oil of thyme. Watery sprays containing from 1 to 2 per cent of ephedrine salt (chloride or sulfate) in physiologic solution of sodium chloride, flavored if desired with peppermint or rose water, have a more effective action which is quicker but not so lasting. These sprays, both oily and watery, may be used in an atomizer or dropped into the nose at intervals of from two to twelve hours. Whereas the object of the spray is chiefly to shrink the nasal mucous membrane, it may have an effect on some nasobronchial reflex, but the physiology of such an action is not clear.

Amphetamine produces a similar shrinkage of the nose. It is a volatile substance and a convenient amphetamine inhaler is available. It should be used cautiously, however, because the drug can raise blood pressure and produce marked restlessness in the very young as well as in older persons.

Neosynephrin hydrochloride is a synthetic derivative of phenylethylamine. Like ephedrine it is an active vasoconstrictor and is used locally in the nose, usually in watery solutions containing from 0.25 to 1 per cent of the drug.

Cocaine will shrink the nasal mucous membrane, but no better than other drugs which do not lead to a narcotic habit.

INTRINSIC ASTHMA

Intrinsic asthma comprises an important group of cases in which asthma begins later in life, at the age of 45 or after. The symptoms are often persistent, bearing no relation to changes in season or environment. Whatever the cause, it appears to be "something which the patient carries with him"; it is of "intrinsic" origin. I suspect that "allergy" in the ordinary sense has little to do with the cause of the trouble. Involvement of the sinuses is a part of the picture and not a cause of it. Emphysema is prone to develop, and the ultimate prognosis is not good. Treatment is difficult.

Potassium iodide and sodium iodide are the great standbys in the treatment of asthma, particularly asthma of the intrinsic type. Supposedly, their effect depends on a stimulation of the bronchial mucous glands to make them pour out a larger amount of watery secretion, which serves to dilute and increase the secretion resulting from chronic bronchial infections. Under the influence of potassium iodide, the sputum becomes thinner and can be raised with greater ease. The action of the cilia is increased. Coughing becomes easily productive and diminishes in severity. The dose of potassium iodide and the duration of its use are important for the reason that, whereas the proper amount will stimulate the bronchi, an excess of the drug will irritate them. Not infrequently I have been able to help my patient greatly by omitting the potassium iodide, which was causing an excessive production of thin, stringy, bronchial mucus and thus making the cough worse instead of better. Potassium iodide, however, presents few objections except that it sometimes causes a disagreeable taste in the mouth after prolonged use, and it may cause a pustular eruption of the skin of the upper part of the trunk. Very rare is the patient who is really sensitive to iodide and who cannot take it in small amounts. The dose of the saturated solution (liquor potassii iodidi, N. F.) can be varied from 5 drops once a day to 25 drops four times a day. The average patient with intrinsic asthma or with a chronic bronchitis and emphysema is advised to begin with 10 drops of potassium iodide three times a day and then reduce the dose as the sputum becomes thinner. Occasionally the dose must be increased to 20 drops before any change is observed. Intelligent patients can be taught to regulate their own doses of potassium iodide, to take it when

11. Boothby, W. M.; Mayo, C. W., and Lovelace, W. R., Jr.: One Hundred per Cent Oxygen, J. A. M. A. **113**: 477 (Aug. 5) 1939.
12. Barach, A. L.: The Use of Helium in the Treatment of Asthma and Obstructive Lesions in Larynx and Trachea, Ann. Int. Med. **9**: 739 (Dec.) 1935.
13. Heatly, C. A.: The Pharmacopeia and the Physician: Local Medication of the Upper Respiratory Tract, J. A. M. A. **107**: 1887 (Dec. 5) 1936.

cough becomes harassing and unproductive and then after a day or two to omit it again "until the next time," and so in this way to take it off and on indefinitely.

Whether the action of potassium iodide depends on the potassium or the iodide molecule is uncertain. The fact that sodium iodide is used in some clinics with equal enthusiasm suggests that the iodide is important. In 1938 Rusk and Kenamore [14] described a new therapeutic approach to urticaria. They discussed the influence of potassium on the tactile excitability of the skin and stated that potassium salts have a pharmacologic action similar to that of epinephrine. It may be that the good effect of potassium iodide in asthma depends on the potassium ion rather than on the iodide. The substitution of potassium chloride for sodium chloride in the diet of asthmatic patients offers a new field for experimentation. Furthermore, the suggestion that potassium iodide may be injected intravenously may be more sensible than was first thought. Whereas the drug, when given by mouth, is absorbed so rapidly as to constitute a classic demonstration for the young student of pharmacology, it may well be that by intravenous injection a sufficiently larger quantity is introduced at one time to produce a more definite pharmacologic effect and perhaps to replace the potassium depleted from the tissue cells. For intravenous use the dose advised is one 10 cc. ampule containing 1 Gm., which may be repeated at intervals of from one to three days, if necessary.

Other expectorant drugs may be needed at times. They include ammonium chloride, terpin hydrate and squill. All these have been described in the first series of these papers by Brown.[15]

BRONCHOSCOPY

Bronchoscopy has been described by Weille,[16] and others too, as "life saving" in asthma, since by it a mass of sticky exudate can be sucked out of the bronchi. Since iodized oil is often injected at the time of bronchoscopy to study the bronchi by x-rays, it has been observed by Balyeat,[17] Anderson,[18] Mandelbaum,[19] Criep [20] and others that the iodized oil itself has a good effect on the bronchial infection, and so here is another therapeutic approach to a difficult problem. Iodized poppy seed oil has been instilled into the trachea in doses as large as 20 cc. without difficulty, and often with good results, after suitable local anesthetizing treatment of the pharynx and throat with cocaine and procaine. Multiple instillations are reported in many instances. The details of this treatment are important and the original references should be consulted for them.

OTHER METHODS OF TREATMENT

Many other methods of treatment have been suggested. Calcium has been used in various forms by mouth and by vein. Hydrochloric acid, peptone, histamine and vaccines have all been tried. Nonspecific therapy with vaccines and other substances injected subcutaneously, or rarely intravenously, to produce a "protein shock" with fever is capable of doing good just as it is capable of doing harm. The fact suggests that the effect of many other treatments given under the skin or into the vein is merely "nonspecific" and dependent on a sort of shake-up—a gross disturbance of many physiologic relationships—but what they are or what nonspecific therapy really does is so far not clear. However, it is important to recognize that many treatments given under the skin and stated to be "specific" in that they are given for some preconceived purpose may not be so "specific" after all.

In the meantime, the patient suffers and must be cared for as a whole—not merely as a "case of asthma." Drugs and vitamins may be required for anemia, constipation, loss of appetite, "debility" and lack of proper nutrition. The man who undertakes to treat the patient must be a physician in every sense. He must rid his patient of all sources of irritation, physical and psychologic, and must do everything to put him or her into the best possible physical condition, for then the asthma will be much easier to deal with. Finally, the physician must be certain that the treatment which he advises will not give more trouble than the disease itself.

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14. Rusk, H. A., and Kenamore, B. D.: Urticaria: A New Therapeutic Approach, Ann. Int. Med. **11**: 1838 (April) 1938.
15. Brown, C. L.: The Pharmacopeia and the Physician: The Use of Expectorants, J. A. M. A. **109**: 268 (July 24) 1937.
16. Weille, F. L.: Studies in Asthma: XIV. Bronchoscopy in Asthma, New England J. Med. **205**: 848 (Oct. 29) 1931.
17. Balyeat, R. M.; Seyler, L. E., and Shoemaker, H. A.: The Diagnostic and Therapeutic Use of Iodized Oil in Cases of Intractable Asthma, with Special Reference to Its Use as Contrast Medium and Physicochemical Mechanism on Which Its Therapeutic Value Is Based, Radiology **24**: 303 (March) 1935.
18. Anderson, William: The Treatment of Bronchial Asthma by Intratracheal Injections of Iodized Oil, New York State J. Med. **36**: 1151 (Aug. 15) 1936.
19. Mandelbaum, M. J.: Intratracheal Injection of Iodized Oil, with Analysis of 1,000 Compiled Cases, Including 114 Newly Reported Cases, M. Clin. North America **20**: 907 (Nov.) 1936.
20. Criep, L. H., and Hampsey, T. W.: Therapeutic Value of Iodized Oil in Bronchial Asthma, J. Allergy **9**: 23 (Nov.) 1937.

HORMONES AND VITAMINS IN COSMETICS

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(Concluded from page 1875)

THE RELATIONSHIP OF CERTAIN VITAMINS TO HORMONES

A close physiologic interrelationship is said to exist between certain hormones and vitamins. The various sex hormones are related to vitamin D in their chemical structure, since "cholesterol may be converted into the male sex hormone; the male sex hormone is readily convertible to estrone and this in turn to progesterone. Testosterone is very similar structurally to ergosterol and vitamin D." [97]

Vitamin A has been found to exert an antagonistic action on thyroxine, as has been demonstrated by various experiments in animals and human beings.[98] These investigators have shown that thyrotoxicosis can be cured and prevented with a diet rich in vitamin A. Conversely, hypervitaminosis A could be prevented and cured by ingestion of desiccated thyroid. Since the original work of Von Euler and Klussmann,[98d] it is generally believed that the growth factor which is contained in vitamin A is counteracted by thyroxine, while the accumulation of vitamin A in the liver is inhibited. Furthermore, in experiments with thyroidectomized goats, Fasold and Heidemann [99] have demonstrated that these animals were unable to transform carotene into vitamin A and that the milk from these animals was yellow instead of white.

97. Murlin, J. R.: Vitamins and Hormones, J. Am. Dietet. A. **14**: 397 (June) 1938.
98. (*a*) Abelin, I.: Ueber den Antogonismus A-Vitamin: Thyroxin, Vitaminforsch. **4**: 120, 1935. (*b*) Fasold, H., and Peters, H.: Ueber den Antogonismus zwischen Thyroxin u. Vitamin A, Ztschr. f. exper. Med. **92**: 57, 1933. (*c*) Hoff, Hans: Vitaminstoerungen des Zentralnervensystems und ihre Therapy, Wien. med. Wchnschr. **87**: 605 (June 5) 1937. (*d*) Von Euler, H., and Klussmann, E.: Carotin and Thyroxin, Ztschr. f. physiol. Chem. **213**: 21, 1932.
99. Fasold, H., and Heidemann, E. R.: Ueber die Gelbfaerbung der Milch thyreopriver Ziegen, Ztschr. f. exper. Med. **92**: 53, 1933.

The thyrotropic substance which is produced by the anterior lobe of the pituitary gland has been found to be closely related to vitamin A by Fellinger and Hochstaedt [100] in their experiments with guinea pigs. They found that the thyrotropic hormone had no effect on the thyroid gland when vitamin A was administered.

Vitamin D has been found to be closely related to the parathyroid gland.[97] Each plays an important role in calcium-phosphorus metabolism; the same effects are produced when either one is given in large quantities. There is an increase in the calcium content of the blood and also an increased absorption of calcium through the intestinal mucosa. The hormone of the parathyroid gland stimulates the elimination of calcium and phosphoric acid at the expense of bone tissue,[101] while an intake of vitamin D enhances the adsorption of calcium and phosphorus to bone by means of a better utilization of the calcium contained in food.[98c] A series of experiments with dogs has demonstrated that after the removal of both thyroid and parathyroid glands these animals could be kept normal by means of substitutional therapy with vitamin D.[102] The exact relationship of vitamin D to the thyroid gland must still be demonstrated. It is the opinion of certain investigators [103] that the thyroid protects the aorta and large vessels from the injurious actions of excessive vitamin D.

Vitamin C, which has been identified as ascorbic acid, has been found in the endocrine glands. The ascorbic acid contents have been quantitatively determined by Mendive and Deulofeu,[104] who found that the largest amounts were present in the pituitary gland, the corpus luteum and the adrenals. Murlin [97] has suggested that "quite possibly there will be found in the cortex a substance closely related to ascorbic acid in its action but not identical with it chemically. . . . One might suppose that the substance, which is not ascorbic acid, and which nevertheless has a vitamin C action, might be an intermediary substance in the process of ascorbic acid formation within the gland."

Various investigators have suggested the existence of an antagonistic relationship between vitamin C and the thyroid gland. After the administration of ascorbic acid to patients with exophthalmic goiter and to both normal and thyroidectomized dogs, Löhr [105] observed a reduction of the blood iodine to below normal limits. He also reports marked clinical improvement with no decrease in the basal metabolism of the patients. The suppression of an increased metabolism due to hyperthyroidism with the administration of vitamin C has been reported by Oehme.[106] There appears to be an intimate relationship between vitamin C and the ovary, as has been shown by Giedosz.[107] He found that either the ovarian follicles in scorbutic guinea pigs were completely lacking or, if these follicles were already present, atresia had occurred.

100. Fellinger, K., and Hochstaedt, O.: Ueber die antithyreoidale Wirkung des Vitamins A, Wien. klin. Wchnschr. **49:** 1339 (Oct. 30) 1936.
101. Shelling, D. H., and Hopper, Katherine B.: Bull. Johns Hopkins Hosp. **58:** 137 (March) 1936.
102. Kozelka, F. L.; Hart, E. B., and Bohstedt, G.: Growth, Reproduction and Lactation in the Absence of the Parathyroid Glands, J. Biol. Chem. **100:** 715 (May) 1933.
103. Handovsky, H., and Goormaghtigh, N.: Vitamin D, Thyroid Gland and Arteriosclerosis, Arch. internat. de pharmacodyn. et de thérap. **56:** 376 (Aug. 31) 1937.
104. Mendive, J. R., and Deulofeu, V.: Ascorbinsäure in inneren Druesen: Isolierung aus Hypophyse, Ztschr. f. physiol. Chem. **236:** 208, 1935.
105. Löhr, H.: Beiträge zur Kenntnis des Jodstoffwechsels: I. Arch. f. exper. Path. u. Pharmakol. **180:** 332, 1936.
106. Oehme, C.: Zur antithyreoiden Wirkung der Nebennierenrinde, Klin. Wchnschr. **15:** 512 (April 11) 1936.
107. Giedosz, B., and Rychlik, W. C.: Image histologique des ovaires dans le scorbut expérimental; influence de la folliculine, Compt. rend. Soc. de biol. **123:** 1226, 1936.

Only a brief attempt has been made here to review some of the many relationships between vitamins and hormones. Murlin,[97] in his masterly summary of the subject, states aptly that "vitamins might properly be regarded as exogenous hormones or hormones may be regarded as endogenous vitamins."

MISNOMERS

There have been offered to the public various so-called turtle-oil, glandular and hormone cosmetic preparations, which by their names suggest active properties which they may not possess. When the alleged active ingredients are inert, such claims are false.

Another subject for clarification is the use of the so-called vitamin F in various cosmetic preparations. "Vitamin F" is a concentrate of unsaturated fatty (linoleic and linolenic) acids found in linseed oil, and its classification as a vitamin has not been generally recognized. The efficacy claimed for this ingredient in cosmetics has not been proved.

ABSORPTION OF VITAMINS THROUGH THE SKIN

The percutaneous absorption of certain vitamins has been established by numerous investigators. Hume, Lucas and Smith [2] originally demonstrated that vitamin D could be absorbed from irradiated cholesterol through a small area of unbroken skin in sufficient amounts to supply the needs of the animal. By experiment they supported Hess's theory that the activation of hydrous wool fat by sunlight and its subsequent absorption through the skin is a possible source of vitamin D. Amrhein's [108] experiments in attempting to determine the conditions under which vitamin D could be absorbed through the skin proved that it can be absorbed percutaneously from both animal and mineral oil bases. Von Mallinckrodt-Haupt,[109] as well as Amrhein, found that the application of creams containing irradiated cholesterol caused repair to take place in rachitic rats. More recently, many investigators have corroborated the absorption of vitamin D through the skin.[110]

The evidence concerning the absorption of vitamin A through the intact human skin is rather meager. This may have been due to the difficulty in separating vitamin A from vitamin D and maintaining its stability. The recent isolation of vitamin A by the process of molecular distillation described by Hickman [111] facilitates further experimental investigation. Helmer and Jansen,[112] in their experiments on the absorption of vitamin A through the skin of rats, demonstrated that this vitamin, as contained in halibut liver oil and carotene, is readily absorbed, preventing severe symptoms of vitamin A deficiency in animals. These experiments were repeated by Eddy,[110] who reported the relative merits of local application as compared with oral administration. He found that the growth effect of carotene emulsion applied topically was one third as

108. Amrhein, F. J.: Absorption of Vitamin D from the Skin, J. Am. Pharm. A. **23:** 182 (March) 1934.
109. Von Mallinckrodt-Haupt, A. S.: Ztschr. f. Vitaminforsch. **4:** 16 (Jan.) 1934.
110. Taylor, N. B.; Weld, C. B.; Branion, H. D., and Kay, H. D.: Canad. M. A. J. **24:** 763 (June), **25:** 20 (July) 1931. Laurens, Henry: Physiological Effects of Radiant Energy, New York, Chemical Catalog Company, 1933. Eddy, Walter: Data Bearing on the Effect of Topical Application of Vitamins A and D to the Skin, unpublished data. Helmer, A. C., and Jansen, C. H.: Absorption of Vitamin D Through Skin, Studies Inst. Divi Thomae **1:** 83 (June) 1937. Astrowe, P. S., and Morgen, R. A.: Dermal Absorption of Vitamin D, Am. J. Dis. Child. **49:** 912 (April) 1935.
111. Hickman, K. C. D.: Molecular Distillation, Indust. & Engin. Chem. **29:** 966-979, 1107-1114 (Oct.) 1937.
112. Helmer, A. C., and Jansen, C. H.: Topical Applications of Vitamin A and of Carotene; Absorption of Vitamin A from Halibut Liver Oil, Studies Inst. Divi Thomae **1:** 1, 10 (June) 1937.

efficient as the same amount by direct feeding. These investigators concluded that vitamin A can produce systemic effects by means of topical application.

Eddy and Howell [112a] conducted additional tests to demonstrate vitamin A absorption through the unbroken skin. Six series of rats, each first depleted of vitamin A by the use of the U. S. P. basal diet, were employed for the tests. The vitamin product was rubbed into the skin over an area and allowed to remain for a specified number of minutes. They concluded that both carotene and vitamin A were absorbable by the intact rat skin in sufficient quantity to stimulate growth but that the carotene was better absorbed than vitamin A.

Regarding the percutaneous absorption of vitamin A in animals, Getz [113] states: "I feel convinced that the absorption through the skin is comparable to the speed of absorption through the gastrointestinal tract."

The lipoid solubility of vitamins A and D is considered the important factor in cutaneous absorption. However, Kasahara and Kawashima [114] have reported that the water-soluble vitamin C can also be absorbed through the human skin, as evidenced by the increase of vitamin C in mother's milk following the application of a 30 per cent solution of ascorbic acid on the skin of the mammae.

SYSTEMIC EFFECTS FROM EXCESSIVE DOSES

There are numerous reports in the literature on the toxicity [115] of vitamin D when administered orally or subcutaneously in excessive doses. The pathologic changes, however, depend on the preparation used, the method of administration, the sensitivity of the experimental animal and the susceptibility of the species. Schuebel [116] reports that guinea pigs show the least amount of reaction to large doses of vitamin D, while cats and rats are the most sensitive. One large dose (10 mg. per kilogram) of irradiated ergosterol has caused death in cats and rabbits. A daily dose of 0.2 mg. of irradiated ergosterol is well tolerated by the white mouse, but 0.6 mg. leads to loss of weight, and 1 mg. was fatal in twenty days. There are many reports [117] of deaths occurring in animals from D-hypervitaminosis. The toxic symptoms are anorexia, loss of weight, accelerated breathing, somnolence, diarrhea and increase in the calcium metabolism. The fur becomes stiff; characteristic calcium deposits are seen in the vascular walls, the heart muscles, the stomach wall, the lungs and the diaphragm. The spleen is frequently atrophic and the small intestine shows signs of hemorrhagic inflammation and ulceration.[117b]

Important and striking symptoms of D-hypervitaminosis are the decalcification of the bones [118] combined with hypercalcemia [119] and deposits of calcium in the internal organs and large vessels.[120]

Kleinschmidt [120a] believes that there is no danger of overdosage in the administration of vitamin A in man. In his animal experiments, however, he found that overdosage may be followed by manifestations resembling those of vitamin A deficiency and that very high overdosage of vitamin D may damage bones and vessels resembling other disturbances of calcium and phosphorus metabolism.

It is interesting to note that parenteral and intraperitoneal injections of irradiated ergosterol are more effective than feeding by mouth. The toxin apparently becomes weakened in the gastrointestinal tract.[116]

Okushima [121] recently performed a very interesting set of experiments in which rabbits suffering from D-hypervitaminosis showed atrophic lesions in the nasal tissues resembling those seen in human cases of rhinitis atrophicans. Gordonoff and Zurukzoglu,[11] also Moncorps, Droller and Carter,[11] have demonstrated symptoms of vitamin D poisoning by rubbing an ointment containing this vitamin into the skin of normal rabbits.

Human D-hypervitaminosis occurs more frequently in children. Several deaths of children have been attributed to an overdosage of vitamin D. Bamberger and Spranger [122] describe parenchymatous nephritis in a child whose death resulted from vigantol poisoning. Vigantol is a German brand of irradiated ergosterol. Park [122a] states that "the idea that vitamin D in the form of irradiated ergosterol is an extremely toxic substance was derived from the use of the old German preparation vigantol, in the wake of which metastatic calcification was observed by a variety of investigators." Thatcher [123] reports the death of an 11 months old child following calcification of the kidneys from overdoses of cod liver oil and vitamin D. Gerlach [124] cites a child's death due to an overdose of vitamin D concentrate. Thomasen [125] reports a case in which calcification of the arteries occurred in a boy aged 8 years who had been treated with vitamin D for febrile inflammation of the joints. The bony structure, calcium content of the blood serum and blood cholesterol were found to be normal in this case. Some of the warning symptoms of the toxic condition are sudden anorexia and loss of weight, accompanied by severe diarrhea and nausea. Tenderness of the gums and teeth, pains in the muscles and joints, headaches, dizziness, paresthesia in the extremities, neuralgia of the trigeminal nerve and the

112a. Eddy, Walter H., and Howell, Joan L.: Topical Application of Vitamin A: Efficiency Judged by Growth Stimulation, New York State J. Med. **39**: 406-410 (March 1) 1939.

113. Getz, H. R., University of Wisconsin, Dept. of Pathology: Personal communication to the authors, May 17, 1938.

114. Kasahara, M., and Kawashima, K.: The Resorption of Vitamin C Through the Skin, Klin. Wchnschr. **16**: 135 (Jan. 23) 1937.

115. Bills, C. E.: Physiology of the Sterols Including Vitamin D, Physiol. Rev. **15**: 1 (Jan.) 1935. György, P.: Sind die bisher üblichen Gaben von bestrahltem Ergosterin als überflüssig Loch zu bezeichnen? Klin. Wchnschr. **8**: 684 (April 9) 1929. Putschar, W.: Ueber Vigantolschädigung der Niere bei einem Kinde, Ztschr. Kinderh, **48**: 269, 1929.

116. Schuebel, Konrad: Zur Toxikologie der Vitamine, Med. Welt. **11**: 705 (May 22) 1937.

117. (*a*) Pfannenstiel, W.: Summary of Recent Work on Vigantol (Irradiated Ergosterol), Lancet **2**: 845 (Oct. 20) 1928. (*b*) Kreitmair, H., and Moll, L.: Hypervitaminose durch grosse Dosen Vitamin D, München. med. Wchnschr. **75**: 637 (April 13), 1113 (June 29) 1928. (*c*) Ammon, R., and Dirscherl, W.: Fermente, Hormone, Vitamine, Leipzig, Georg Thieme, 1936. (*d*) Harris, L. J., and Moore, Thomas: Hypervitaminosis and Vitamin Balance; Instance of Vitamin Balance, Biochem. J. **23**: 1114, 1929.

118. Guldager, A.: D-Hypervitaminosis Illustrated by Quantitative Experiments in Overdosing, Dissertation, State Vitamin Laboratory, Copenhagen, 1926. Reed, C. I.; Dillman, L. M.; Thacker, E. A., and Klein, R. I.: The Calcification of Tissues by Excessive Doses of Irradiated Ergosterol, J. Nutrition **6**: 371 (July) 1933.

119. Harris, L. J., and Innes, J. R.: The Mode of Action of Vitamin D: Studies on Hypervitaminosis D, Biochem J. **25**: 367, 1931. Shelling, D. H., and Asher, D. E.: Calcium and Phosphorus Studies: IV. The Relation of Calcium and Phosphorus of the Diet to the Toxicity of Viosterol, Bull. Johns Hopkins Hosp. **50**: 318 (May) 1932.

120. Duguid, J. B.: Vitamin D Sclerosis in the Rat's Aorta, J. Path. & Bact. **33**: 697 (July) 1930. Ham, A. W., and Lewis, M.D.: Experimental Intimal Sclerosis of the Coronary Arteries of Rats, Arch. Path. **17**: 356 (March) 1934. Schmidtmann, J.: Centralbl. f. allg. Path. u. path. Anat. **43**: 8, 1928. Herzenberg, H.: Studien über die Wirkungsweise des bestrahlten Ergosterins (Vigantol) und die Beziehungen der von ihm gesetzten Veränderungen zur Arteriosklerose, Beitr. z. path. Anat. **82**: 27 (June 29) 1929.

120a. Kleinschmidt, Adolf: Ueber Vitamine und Hormone, Fortschr. d. Med. **56**: 250, 1938.

121. Okushima, H.: Experimental Studies on the Effect of Overdosage of Vitamin D on the Nasal Tissues, Mitt. a. d. med. Akad. zu Kioto **20**: 1729, 1937.

122. Bamberger and Spranger: Vigantol bei tuberkulosen Kindern, Deutsche med. Wchnschr. **54**: 1116 (July 6) 1928.

122a. Park, Edwards A.: The Use of Vitamin D Preparations in the Prevention and Treatment of Disease, in The Vitamins, a symposium published by the American Medical Association, Chicago, 1939.

123. Thatcher, L.: Hypervitaminosis D, Lancet **1**: 20 (Jan. 4) 1936.

124. Gerlach, W.: Zur Frage der Vitamin-D-Sklerose beim Menschen, München. med. Wchnschr. **83**: 49 (Jan. 10) 1936.

125. Thomasen, Eivind: Calcification of Arteries in a Boy 8 Years Old, Resulting from Vitamin D Treatment, Acta med. Scandinav. **93**: 505, 1937.

like have been described as symptoms of D-hypervitaminosis in human beings.[126]

Pfister[10] reported cutaneous manifestations resulting from overdosage of vitamin D solutions given orally, describing these as a fine papular rash superimposed on an erythematous base resembling an early eczema. It usually occurred on the face. Two cases of severe skin eruptions in children who were accidentally given overdoses were reported. There was immediate cessation of the condition when administration of the vitamin was discontinued. Pfister explained:

> These two cases, of course, are the extreme both in dosage and in the severity of the rash. My experience with skin conditions associated with vitamin overdosage has prompted me to be on the lookout for this manifestation, and I have encountered many facial rashes of varying degrees of severity which have cleared up after the vitamin solution was discontinued and the dosage later adjusted. I have reported these observations at a medical society meeting and have received several letters from physicians in the nearby towns who had noted several cases that cleared up after the vitamin solution had been stopped or the dosage adjusted.

An extensive review of the many experiments proving the toxic effects of vitamin D shows a great variability in the toxic threshold. In animals the approximate toxic dosage has been reported to be several thousand times the therapeutic dose. Rosenheim and Webster[127] reported that 10,000 times the minimum antirachitic dose was not lethal to rats. Collazo, Rubino and Varela[128] observed that rats died within six weeks when fed the McCollum high calcium rickets-producing diet 3143, plus 50,000 times overdosage of activated ergosterol. Bills and Wirick[129] in a study involving large numbers of rats from infancy to late maturity found that 1,000 times overdosage was just perceptibly harmful, 4,000 times overdosage definitely injurious and 40,000 times overdosage strongly toxic to rats receiving a normal diet. Bills[115] explained that the margin of tolerance for man has not been as accurately determined as for the rat, but it is probably not so great. Bills cites Crimm and Reed, who indicate that in man toxic effects begin to appear when approximately 600,000 international units, or 200 times the ordinary dose, of properly irradiated ergosterol is administered daily over a period of several weeks.

A-hypervitaminosis in animals has also been reported, causing emaciation, loss of weight, loss of hair, hypertrophy of the thyroid gland, fatty degeneration of the liver and hemorrhages in the lungs and intestine, finally leading to the death of the animal. Schuebel[116] reported that relatively small amounts of vitamin A (2,000-10,000 U. S. P. units) decreased the metabolism of normally fed guinea pigs and rats by from 9 to 16 per cent and that 20,000 units daily led to symptoms of hypervitaminosis after five days. Some of the symptoms described were spastic contraction of the extremities, diarrhea, hemorrhagic rhinitis, conjunctivitis, exophthalmos and the tendency to spontaneous fractures. Autopsy revealed necrotic glomerulonephritis with calcification, fatty infiltration of the liver and parenchymatous damage of the spleen. Similar experiments were performed by Bommer[130] and by Ammon and Dirscherl,[117c] which demonstrated the same pathologic changes in rats and mice.

Excessive administration of vitamin A concentrates to experimental animals has been reported to result in damage to bone, kidneys, skin and other soft tissue. However, no injury is likely by use of the usual liver oils in high dosage.[130a]

Sherwood, Brend and Roper[131] observed the effect of hypervitaminosis on the vaginal smears of rats, and their work was later enlarged on by Sherwood, Depp, Birge and Dotson,[132] who demonstrated the effect of excessive administration of vitamin A on the estrous cycle. These investigators concluded that there was a disturbance in the estrous cycle as indicated by the study of the uteri and ovaries, as well as the vaginal smears, after vitamin A had been administered in excessive amounts orally and subcutaneously in the form of carotene. Bessey and Wolbach[133] reported that the estrous cycle may also be affected by vitamin A deficiency:

> The changes in the repair of epithelium after vitamin A deficiency have their normal counterpart in changes in the vagina of rodents during the part of the estrous cycle in which the cornified vaginal epithelium returns to the mucous type.

Symptoms of A-hypervitaminosis have not as yet been observed in man. Ammon and Dirscherl[117c] state that the possible danger of overdosage of vitamin A is diminished because of the lower degree of solubility of carotene in oil.

It has been proved by animal experiments that a simultaneous feeding of water-soluble and fat-soluble vitamins in extremely large doses could not produce hypervitaminosis. This led to the conclusion that there exists some sort of antagonism in which the effects of the fat-soluble vitamins may be counteracted by the water-soluble vitamins.[116]

EFFECTS OF TOPICAL APPLICATION

The employment of vitamin D in the form of fish oil (cod liver oil) was discovered by the inhabitants of fishing communities. They rubbed cod liver oil on the skin of children in order to cure and prevent many types of local and generalized diseases. Interest in the topical application of cod liver oil on the skin has been aroused by numerous clinical experiments in the treatment of burns and wounds.[134] Third degree burns and infected wounds were successfully treated with applications of cod liver oil.

Massot[134a] treated an x-ray ulcer of the hand by means of an ointment containing vitamins A and D. He reported that the pains disappeared after the first week of treatment and that the ulcer was healed after

126. Crimm, P. D.: Vitamin Therapy in Pulmonary Tuberculosis: Treatment of Pulmonary Tuberculosis by Means of Hypercalcemia Induced by Massive Doses of Activated Ergosterol, Am. Rev. Tuberc. **26:** 112 (Aug.) 1932. Crimm, P. D.; Strayer, J. W.; Watson, H. L., and Heimann, G.: Vitamin Therapy in Pulmonary Tuberculosis: Effect of Viosterol on Absorption, Retention and Excretion of Calcium, ibid. **28:** 202 (Aug.) 1933.

127. Rosenheim, O., and Webster, T. A.: The Parent Substance of Vitamin D, Biochem. J. **21:** 389, 1927.

128. Collazo, J. A.; Rubino, P., and Varela, B.: Experimentelle Hypervitaminose der Ratten durch grosse Dosen bestrahlten Ergosterins, Biochem. Ztschr. **204:** 347, 1929.

129. Bills, C. E., and Wirick, A. M.: Long-Time Feeding Experiments with Activated Ergosterol, J. Biol. Chem. **86:** 117 (March) 1930.

130. Bommer, S.: Skin and Vitamins, Deutsche med. Wchnschr. **60:** 570 (April 13) 1934.

130a. Bessey, Otto A., and Wolbach, S. G.: Vitamin A—Physiology, Pathology, in The Vitamins, Chicago, American Medical Association, 1939.

131. Sherwood, T. C.; Brend, M. A., and Roper, E. A.: Changes in the Vaginal Epithelium of the Rat on an Excessive Vitamin A Diet, J. Nutrition **11:** 593 (June) 1936.

132. Sherwood, T. C.; Depp, O. R.; Birge, G. P., and Dotson, H. B.: Further Studies on the Effect of Excessive Vitamin A on the Estrous Cycle of the Rat, J. Nutrition **14:** 481 (Nov.) 1937.

133. Bessey, O. A., and Wolbach, S. B.: Vitamin A: Physiology and Pathology, J. A. M. A. **110:** 2072 (June 18) 1938.

134. Löhr, W.: Treatment of Burns with Cod Liver Oil, Chirurg. **6:** 263 (April 1) 1934; Cod Liver Oil Salve Treatment of Wounds and Burns, Zentralbl. f. Chir. **61:** 1815, 1934. Löhr, W., and Treusch, K.: Effect of Cod Liver Oil on Pyogenic Bacteria, ibid. **61:** 1807 (Aug. 4) 1934. Boltán, L.: Vitamine in der Wundebehandlung, ibid. **62:** 3031 (Dec. 21) 1935. Getz, H. R.: Cod Liver Oil Therapy in Experimental Tuberculosis, unpublished data.

134a. Massot, M. H.: Guérison rapid d'une radiodermite ulcéreuse tardive par une préparation à base de vitamines A et D, Bull. soc. franç. de dermat. et syph. **45:** 1842 (Dec.) 1938.

four weeks. In the discussion following Massot's report, Milian mentioned a similar result with "oil de Flétan."

Dainow [134b] treated occupational dermatitis by means of parenteral injections of vitamins A and D and local application of vitamin D in some of his cases. He reported that he not only cured seventeen out of eighteen patients but also obtained a complete desensitization. He concludes that the tolerance of the skin for certain substances is related to its vitamin A and D contents.

De Grosz [134c] advocates the local application of vitamin A in the form of oil or ointment in ophthalmic practice. "It is extremely useful in promoting epithelization of fresh corneal lesions." He recommends, however, that the treatment include the internal use of the same preparation for the best results. "The therapeutic use of the vitamin ointment is also indicated in caustic burns of the conjunctiva, chronic eczema, ulcers, inflammation of the lids, etc., and in acute photo-ophthalmia, herpes of the cornea, neurotrophic conditions, and gonorrheal ulcers. Overdosage, which may produce necrosis of epithelium, must be guarded against."

Lauber [135] observed in animal experiments that the local application of vitamin A produces no acceleration in the process of wound healing. He states that vitamin D produces a slight acceleration of the healing process when administered in low concentration and no effect when given in moderate doses and that concentrated doses of vitamin D retard the healing process. Löhr and Unger [136] also mention that a concentration of vitamins higher than that present in the natural state of cod liver oil retards rather than accelerates the healing of wounds.

Many other investigators have confirmed the work of Löhr, in the treatment of wounds, ulcers and boils with cod liver oil. Getz,[134] in a recent preliminary report, observed a favorable healing action on tuberculous ulcers in guinea pigs, which indicated a specific effect of the vitamin fractions A and D contained in oil. In determining the efficacy of vitamins A and D, and also of the saponifiable and nonsaponifiable portions of oils containing these vitamins, he used 1,400 guinea pigs which had been inoculated with virulent tubercle bacilli producing tuberculous ulcers of the skin. In his first experiments, in which he used cod liver oil applied topically to the lesions and repeated six times, healing progressed at a much more rapid rate than in the controls. After chemical fractionation of the oil he found that the fatty acid fraction had the same effect as rancid oils; that is, irritation with no healing. He therefore concluded that "the active agent is concentrated in the nonsaponifiable residue since it causes healing more rapidly than the whole oil, often as early as the twelfth day of treatment, with remarkably little scar tissue." It was also found that cod liver oil in these experiments produced a systemic effect, since the treated animals showed less generalized tuberculosis than the controls.

In continuing the aforementioned experiments, Getz reported that the nonsaponifiable residue administered either topically or intramuscularly exerted a similar but more marked effect. Further fractionation into the sterols and the vitamin fraction proved that it was the vitamin fraction which was the effective agent in healing. Since the vitamin fraction contains vitamins A and D, he continued his experiments in order to determine which vitamin was the more efficacious. By using three different fish liver oils in which the proportions of A and D varied, he showed that cod liver oil, which contains a greater percentage of vitamin D in proportion to vitamin A than the other oils, was the superior healing agent.

Löhr and Unger,[136] after some 500 experiments on guinea pigs, concluded that cod liver oil is effective in accelerating the healing of wounds. A favorable influence was exerted by vitamins A and D. They reported that the components of cod liver oil had a general as well as a local action, and they regarded the stimulating effects of the vitamins on the healing of wounds as a result of catalytic action in oxidizing cell processes. Local applications of vitamin C also facilitated the healing process.

Claussen,[136a] discussing the local treatment of infections, burns and fresh wounds with application of oils containing cod liver oil or concentrates, doubts any specific action of vitamins contained in such preparations applied locally.

Lichtenstein [136b] has recently completed a study on the bactericidal properties of cod liver oil. He concludes that there can be little doubt that the striking results obtained with cod liver oil dressings are, at least in part, due to the bactericidal power of the oil. Thus, dressings soaked with cod liver oil, or the application of a thick layer of cod liver oil ointment in the local treatment of infected wounds, burns, ulcers, osteomyelitis or amputation stumps, which have been advocated for about seven years, seem to be of value through the local growth-promoting and stimulating action of vitamins A and D, the absorption of these vitamins into the general circulation, and the observed detoxicating effect of cod liver oil on bacterial toxins.

The therapeutic systemic effect of vitamin D when applied topically is indubitable. The practicability of the cutaneous application as compared with oral administration, however, is questionable, except in cases in which ingestion is not possible, as the amount required for this form of therapy would necessitate many times the recognized oral dose of vitamin D.[137] This would not be a very economical method for treating a systemic disorder.

There is no conclusive experimental evidence proving local effects after local application of vitamins A and D to the unbroken skin, even in large quantities. Up to the present there has been no available evidence of any toxic effect in man after the topical application of vitamins contained in ointment.

VITAMINS A AND D IN VITRO

Several attempts have been made to demonstrate the effects of the fat-soluble vitamins on epithelial cells in tissue culture. In a recent report by Eddy,[138] mention is made of experiments performed by Dalldorf and Rowe in which tissue cultures of epithelium from chick embryo iris were grown in a medium of chicken plasma plus chick embryo extract, and in a medium depleted of vitamin A content plus chicken embryo extract. With the same technic, tests were also run in which

134b. Dainow, I.: Traitement des dermites professionelles par les vitamines A et D, Acta dermat.-venereol. **20**: 191 (March) 1939.

134c. De Grosz, Stephen: Local Use of Vitamin A Preparations in Ophthalmic Practice, Arch. Ophth. **22**: 727 (Nov.) 1939.

135. Lauber, H. J.: Influence of Vitamins on Acute Infections, Beitr. z. klin. Chir. **158**: 633, 1933.

136. Löhr, W., and Unger, F.: Tierexperimentelle Untersuchungen über die Wundheilung mit Lebertran und die Wirkung seiner Bestandteile, Arch. f. klin. Chir. **189**: 405, 1937.

136a. Claussen, S. W.: The Pharmacology and Therapeutics of Vitamin A, in The Vitamins, Chicago, American Medical Association, 1939.

136b. Lichtenstein, M.: Cod Liver Oil Dressings: Their Mode of Action, Lancet **2**: 1023 (Nov.) 1939.

137. Dermal Absorption of Vitamin D, editorial, J. A. M. A. **105**: 36 (July 6) 1935.

138. Eddy, Walter: Experiments on the Effect of Vitamins A and D When Brought into Actual Contact with Living Epithelial Cells, unpublished data.

the normal medium was reinforced with calciferol in an amount to supply 1,000 units of vitamin D per cubic centimeter of plasma. The results of these experiments showed that the addition of vitamin A will maintain the growth of epithelium which is depleted of both vitamins A and D, while vitamin D alone did not maintain this growth. They also demonstrated that vitamin A increases the growth of both epithelium and connective tissue; that the addition of vitamin D increases the growth of epithelium but only if A is present to a measurable amount. The growth rate of connective tissue is not influenced by vitamin D.

From these experiments in vitro it would be rather difficult to attempt an analogous appraisal of the effects of these vitamins in vivo. It has not been ascertained that the biologic condition of the surrounding plasma medium for the isolated epithelial animal cells is identical with that of human epithelial tissue in the living organism. Thus these observations can serve to describe the effect of the fat-soluble vitamins only on isolated tissues taken from living animals.

THE EFFECTS OF VITAMIN DEFICIENCIES ON THE SKIN

While no characteristic skin manifestations have been observed in vitamin D deficiency, many specific skin lesions have been ascribed directly to A-avitaminosis.

A direct effect of vitamin D on the vitality and respiration of the skin has been described by Presnell,[139] who proved that vitamin D deficiency reduces the respiratory action of the skin in rats. He states that it cannot as yet be determined "whether this effect is a direct one, the vitamin acting on the calcium-phosphate metabolism of the skin, or an indirect one, through change in the blood calcium and phosphorus, or through the thyroid or other internal secretion."

The vitamin A deficiency principally affects the epithelial structures. The chief symptoms are lesions of the eye, retarded growth and pathologic changes in the epithelium of the respiratory, alimentary and genito-urinary tracts. The cutaneous lesions of vitamin A deficiency are usually described as a dryness of the skin due to an increase in keratinization, with keratotic papular lesions arising from the pilosebaceous follicles. Microscopic examination of the individual lesions reveals a distention of the follicular orifice with plugging of the latter by cornified epithelium. There is usually a hyperplasia of the epidermis together with atrophy of the appendages of the skin. The lesions are most frequently localized on the trunk and extremities.[140]

Mathews[141] comments on vitamin A deficiency as follows:

> Among the earliest symptoms of a deficiency of vitamin A at present recognized in adult humans is a skin disease known as "phrynoderma" or "toad skin." The earliest symptoms are dryness of the skin followed by a papular eruption. It was cured by cod liver oil.

Scheer and Keil,[140] in a review of the cutaneous manifestations in vitamin deficiencies, have concluded that the earliest lesion of vitamin C deficiency (scurvy) appears to be clinically indistinguishable from that observed in vitamin A deficiency. While both diseases attack the hair follicles, the fundamental processes appear to be different. The advanced follicular lesion of scurvy is more easily differentiated from the keratinization processes in A-avitaminosis, the vascular factor connected with vitamin C deficiency being the distinguishing characteristic, in contrast to the effect of vitamin A deficiency on the epithelium and the hair follicles. Scheer and Keil cite cases of follicular papules, hyperkeratoses and scurvy which were described in 1918 and 1919 by Nicolau and by Wiltshire.

That the symptoms of vitamin deficiency disappear when the necessary vitamins are restored orally is a known and accepted fact. Wolbach[142] states that the potentialities of the cells are not lost and that chemical roles are suppressed but proliferative powers are not inhibited when the vitamin deficiency is restored to the animal by the necessary amount of vitamin A.

Vitamin A deficiency in experimental animals has been repaired by means of topical applications, as demonstrated by Helmer and Jansen.[112] They were able to prevent the severe symptoms of A-avitaminosis by rubbing vitamin A on the skins of rats. There is no experimental evidence available as yet proving any similar successful therapy with the local application of the vitamin in man. The local influence of this vitamin, when applied topically directly on the cutaneous lesions arising from vitamin A deficiency, has not as yet been demonstrated in either animals or human beings.

VITAMINS AND EXPERIMENTAL TUMORS

Many attempts have been made to associate the influence of vitamins with the development of experimental tumors in different animals. Barbiroli[143] performed several experiments with subcutaneous injections of "vigantol" (irradiated ergosterol) using the Ehrlich mouse carcinoma. In only one experiment was he able to demonstrate an effectual influence on tumor growth. Burrows and Mayneord[144] were able to produce spindle cell sarcomas in mice after the subcutaneous injection of cholesterol which had been irradiated with roentgen rays. Combining the results of their own investigations with those recorded by others, Ludwig and von Ries[145] concluded that both vitamins and hormones exert a definite effect on malignant neoplasms. They stated that deprivation of vitamin inhibits tumor growth. Geréb[146] also demonstrated that the development of cancer metastases and recurrences was facilitated by the excessive administration of vitamins A, B, C and D in the diet of white mice painted with tar. A vitamin-deficient intake had the opposite effect. Variations in the amount of the single vitamins produced no changes. The same results were obtained by Davidson,[147] who concluded after six years of study on 600 mice that a diet rich in vitamins A, B and E raises the tumor threshold in tar carcinoma while a lack of these vitamins lowers it.

139. Presnell, J.: Experimental Proof That Vitamin D Deficiency Reduces the Respiratory Action of the Skin, Biochem. J. **121**: 5 (Oct.) 1937.

140. Frazier, C. N., and Hu, C. K.: Cutaneous Lesions Associated with Deficiency in Vitamin A in Man, Arch. Int. Med. **48**: 507 (Sept.) 1931. Loewenthal, L. J. A.: A New Cutaneous Manifestation in the Syndrome of Vitamin A Deficiency, Arch. Dermat. & Syph. **28**: 700 (Nov.) 1933. Scheer, Max, and Keil, Harry: Follicular Lesions in Vitamin A and C Deficiencies, ibid. **30**: 177 (Aug.) 1934. Jehgers, Harold: The Degree and Prevalence of Vitamin A Deficiency in Adults, J. A. M. A. **109**: 756 (Sept. 4) 1937.

141. Mathews, A. P.: Vitamins, Minerals and Hormones, Baltimore, William Wood & Company, 1937.

142. Wolbach, S. B.: The Pathologic Changes Resulting from Vitamin Deficiency, J. A. M. A. **108**: 7 (Jan. 2) 1937.

143. Barbiroli, M.: Influence of Vigantol on Experimental Tumors, Tumori **8**: 101, 1934.

144. Burrows, Harold and Mayneord, W. V.: A Note on Tumors in Mice Following Injection of Irradiated Cholesterol in Lard, Am. J. Cancer **31**: 484 (Nov.) 1937.

145. Ludwig, F., and von Ries, J.: Hormones, Vitamins, Cell Growth and Carcinoma, Schweiz. med. Wchnschr. **64**: 141 (Feb. 17) 1934.

146. Geréb, P.: Tar Tumors and Vitamins, Tumori **10**: 177, 1936.

147. Davidson, J. R.: An Attempt to Inhibit the Development of Tar Carcinoma in Mice: III. The Effect of Vitamins on the Tumor Threshold, Canad. M. A. J. **37**: 434 (Nov.) 1937.

Cameron and Meltzer,[148] also Gordonoff and Ludwig,[149] report on the relation of vitamins to carcinoma.

According to Schuebel,[116] it appears quite certain that the growth and development of tumors is stimulated in D-hypervitaminosis. There even seems to be a tendency to the formation of malignant growth. He cites Caspari and Ottensooser, who found a marked increase in growth in the inoculation tumors of white mice which had been fed "vigantol" every third or fourth day.

Guggisberg,[150] in a general review, points out that no dietary element, including vitamins, has any specific connection with malignant growth, though vitamin excess is one factor in the initiation of a neoplasm. He warns against the overwhelming amounts of vitamins now recommended by misguided enthusiasts, for he states that, while vitamins may not actually initiate cancer, they may favor its development by stimulating the growth of degenerating cells, particularly in the higher age periods.

A series of experiments[151] has been performed on rats with the oral administration of crude wheat germ oil, which has been described as a source of vitamin E. Spindle cell sarcomas developed in the abdominal cavity and transplants of these malignant tumors were successful. The nature of the sarcogenic agent has not as yet been determined, and it is not known whether it is inherent in the germ or produced in the process of extraction of the oil. Rowntree,[152] referring to his work on this subject, says:

> We have never produced tumors with vitamin E, but we have seen intra-abdominal development of sarcoma as a result of feeding of the ether extract of wheat germ oil. Such tumors have been produced in a large series of rats.

A complete review of this subject has been made by Bacharach,[153] who concludes that the previously described experiments were obtained with only one sample of oil out of several, and since the results did not follow the feeding of equivalent quantities of the nonsaponifiable portion in the same oil, it is almost certain that they cannot be attributed to its vitamin E content. He states that experiments with solvent-extracted wheat germ oil have failed to show the slightest evidence of tumor production.

The only conclusion to be drawn from a review of the numerous experiments to determine the relationship between tumors and vitamins is the possibility of inhibiting the growth of experimental tumors in animals by means of a diet lacking in vitamins. The evidence that experimental tumors can be produced by a diet rich in vitamins is inconclusive.

VITAMINS IN COSMETICS

Previously it has been indicated that certain vitamins (A, C, D) may be absorbed through the intact skin. Redgrove[4] points out that the real question at issue is not the ability of the skin to absorb these substances but "whether when so absorbed the vitamins exercise any beneficial action on the skin—in short, whether they are of any cosmetic value."

It is the opinion of several investigators[154] that the use of vitamins in soap has no value locally or systemically. Killian[8] suspended rachitic rats in a 5 per cent solution of soap containing 1,300 U. S. P. units of vitamin D per hundred grams for one hour daily over a period of from ten to twenty-one days, with the necessary control animals. There was no evidence of the healing of rickets. Another experiment by the same investigator consisted of the application of gauze pads soaked with the vitamin soap on the shaved abdomens of rachitic rats, which also showed no therapeutic effects after twenty-one days. Durfee[9] wrote:

> In a general consideration of the entire question of the value of the vitamins in cosmetics and toilet preparations one fact must be kept in mind. The results on which the above conclusions have been based have only covered materials that are allowed to remain on the site of application. Most of the materials used were applied by rubbing them into the skin. In view of the fact that soaps only remain in contact with the skin under practical conditions for a minute or two at most, it is questionable whether much absorption can take place during the actual washing operations. Some work has appeared in the literature to indicate that irrespective of the amount of rinsing a thin film of oil from the soap does remain on the skin. However, this film would be so slight as to permit the utilization of only a small percentage of the vitamin.

A complaint issued by the Federal Trade Commission in the *Drug Trade News,* June 21, 1937, is also quoted in THE JOURNAL as follows:

> In truth and in fact said statements and representations were and are false and misleading in that it is impossible for the skin to absorb an appreciable amount of vitamin by simply washing with soap or taking a lather bath. Further, vitamin D has no effect whatsoever upon the skin.

Mention should also be made of the questionable vitamin F. The Toilet Goods Association,[5] in its bulletin for the industry, declared:

> The inclusion of this substance in cosmetics would not appear in the light of our present knowledge to have any substantial scientific approval, except in cases where humans have been on an "essential fatty acid deficiency diet" and it is indeed hard to conceive of such a diet among cosmetic users, or in fact, among any other adult human beings eating the usual American food.

Goodman,[155] in discussing vitamin F says that:

> The status of the isomerized linoleic and linolenic esters which are claimed to be part or all of the active ingredients of the so-called vitamin F has not been sufficiently established by nonpartisan observers. The main claim for so-called vitamin F in mineral oil as a cosmetic is that it prevents certain types of dermatitis of the tail of a rat. The effect on human beings of the application of vitamin F to the skin is doubtful at this writing.

Bacharach,[156] after a review of the literature on the essential unsaturated fatty acids, said that there was a lack of any established facts to justify recommendation of vitamin F to the public for external application to the skin in the form of cosmetics.

The Bureau of Investigation of the American Medical Association,[157] referring to "vitamin F (?)" in cosmetology, declared: "There was thus no substance designated by recognized scientific organizations as vitamin F."

148. Cameron, A. T., and Meltzer, S.: The Effects of Certain Diets on the Production of Tar Carcinoma in Mice, Am. J. Cancer **30:** 55 (May) 1937.

149. Gordonoff, T., and Ludwig, F.: Importance of Vitamins in Therapy of Cancer, Ztschr. f. Krebsforsch. **46:** 73, 1937.

150. Guggisberg, Hans: Vitamins, Hormones and Cancer, Schweiz. med. Wchnschr. **65:** 857 (Sept. 7) 1935.

151. Rowntree, L. G.; Steinberg, A.; Dorrance, G. M., and Ciccone, E. F.: Sarcoma in Rats from the Ingestion of a Crude Wheat-Germ Oil Made by Ether Extraction, Am. J. Cancer **31:** 359 (Nov.) 1937. Dorrance, G. M.: Production of Sarcoma in Albino Rats as a Result of Feeding Crude Wheat-Germ Oil, Proc. Soc. Exper. Biol. & Med. **36:** 426 (April) 1937. Rowntree, L. G.; Lansbury, J., and Steinberg, A.: Neoplasma in Albino Rats Resulting from the Feeding of Crude Wheat-Germ Oil Made by Ether Extraction, ibid. **36:** 424 (April) 1937.

152. Rowntree, L. G.: Personal communication to the authors.

153. Bacharach, A. L.: Recent Research on Vitamin E, Glaxo Laboratories Ltd., Greenford, Middlesex, England.

154. Borsook.[4] Killian.[8] Durfee.[9]

155. Goodman, Herman: Cosmetic Dermatology, New York, McGraw-Hill Book Company, 1936.

156. Bacharach, A. L.: Manufacturing Perfumer, London, April 17, 1937.

157. Rats—and Vitamin F (?) in Cosmetology, Bureau of Investigation, Editorial, J. A. M. A. **108:** 1279 (April 10) 1937.

In a personal communication concerning the beneficial potentialities of vitamins when applied topically, E. M. Nelson,[4] chief of the Vitamin Division, Food and Drug Administration, United States Department of Agriculture, in reply to our query writes:

Most of the studies with which we are familiar deal with preparations containing vitamins A and D. *There appear to be no favorable reports with respect to external application of the other vitamins.* It has been shown that the physiological effects produced by the ingestion of vitamin D can be produced by topical applications of this vitamin to the skin. There appears to be no evidence that vitamin D affects the *skin itself or the immediate underlying tissues.* The evidence as to whether vitamin A can be absorbed through the unbroken skin or not is not clear. . . . We cannot conclude that it has been shown that the beneficial effects reported from the use of these oils are due to the presence of the vitamins. It remains to be demonstrated that the presence of vitamin A or D is even in part responsible for any beneficial effect observed.

Evaluating vitamins in cosmetics, Robertson [158] says:

After a careful review of the literature, we have been unable to find any well substantiated work which would support the contention that the presence of vitamins in cosmetics offers any particular advantage.

Borsook [4] of the California Institute of Technology, in his discussion of vitamins in cosmetics, states that there is no scientific evidence in support of claims that vitamin D enhances the value of cosmetic preparations. He further says:

It is extremely improbable that the vitamin D intake is significantly raised by the amount which is absorbed through the skin from such preparations. There is further no reason to believe that vitamin D rubbed into the skin is any more effective than when taken by mouth. The practice of putting vitamin D into soap—the advertisements refer to it as "the sunshine vitamin"—is even less useful, because the soap does not remain on the face long enough for any of the vitamin to be absorbed.

A warning to the cosmetic industry in the *American Perfumer* [6] of May 1938 reads: "Be careful what you claim for benefits from use of vitamin cream and use a minimum of 250 vitamin D units per ounce. . . ."

Redgrove [4] gives the following opinion:

Many emphatic statements as to their cosmetic utility are to be found in trade and technical literature; but, apart from work demonstrating the utility of cod liver oil and allied products in facilitating the healing of wounds and burns, one seeks in vain for detailed reports of adequately controlled experiments.

The Toilet Goods Association [5] in its bulletin of May 7, 1937, gave out the following information to members of the industry:

There seems no doubt that this substance can be absorbed *through* the skin, but there is no evidence that it is absorbed *by* the skin. . . . Vitamin D applied externally and whether produced by the ultraviolet irradiation of ergosterol or cholesterin, or from one of the fish liver oil concentrates, will in rachitic conditions improve the health of those suffering from vitamin D deficiency. In turn it is quite possible that this may improve the health of the skin as a part of the general health improvement of the patient. . . . However, the external application of this vitamin to adults suffering from a deficiency would not appear to be a satisfactory means of obtaining the required vitamin. . . . Vitamin A (carotene) was not mentioned because it has not yet been shown that it can be absorbed, nor that it has any effect on the skin unless it be taken internally. Carotene mixed with vitamin D in the form of irradiated ergosterol has been found helpful in quickening the healing of wounds with a remarkable lessening of scar formation; however, this of itself does not indicate any great cosmetic value.

McDonough [4] says:

In food chemistry and also in physiological chemistry, tremendous advances have been made in the study of vitamins, but in dermatological chemistry there has not, to my knowledge, been any meritorious work done relative to the effect of vitamins upon the skin.

Finally, a reply from the American Medical Association to an inquiry from the Consumers' Research Bureau [159] brought forth the information that, "while it might be true that vitamin D might be absorbed from the cream, there was no scientific evidence that the absorption would have any cosmetic effect whatever on the skin."

SUMMARY ON VITAMINS

1. It is possible for vitamins D, A and C to be absorbed through the skin.
2. Vitamin D applied to the skin in sufficient amounts has cured rickets in animals and human beings.
3. D-hypervitaminosis has frequently been observed in animals, causing death in some cases. Important and striking symptoms are decalcification of bones combined with hypercalcemia and deposits of calcium in the internal organs and large vessels.
4. The ingestion of excessive amounts of vitamin D may produce parenchymatous nephritis, calcification of the kidneys and arteries, and skin eruptions in human beings. Vitamin D is apparently the only vitamin that may cause toxic symptoms in man when given orally, but no such effects have been reported following cutaneous applications.
5. Small amounts of vitamin D applied on wounds or burns may accelerate the healing process, although large doses retard it.
6. It has been reported that the topical application of vitamin A has corrected the symptoms of A-avitaminosis in animals.
7. In animals, toxic conditions resulting from the ingestion of large amounts of vitamin A have been reported. The symptoms were hemorrhagic neuritis, conjunctivitis, exophthalmos, tendency to spontaneous fractures, necrotic glomerulonephritis with calcification, fatty infiltration of the liver and parenchymatous damage to the spleen.
8. Excessive doses of vitamin A have been found to produce disturbances in the estrous cycle of rats.
9. There is no proof that the topical application of vitamins has any local effect on the intact human skin.
10. A low vitamin intake may retard the growth of tumors. The evidence that hypervitaminosis can accelerate tumor growth is inconclusive.
11. The topical application of vitamins on the skin for the treatment of vitamin deficiency is unpractical and uneconomical. In certain cases in which absorption by ingestion is ineffective and injection is inadvisable, the percutaneous method may be tried.
12. The use of vitamins in creams, lotions and soaps has not been proved to have cosmetic value.

CONCLUSIONS

1. Cosmetics should not contain potent ingredients having constitutional effects. There is a potential danger to normal persons using cosmetics containing active therapeutic substances which, in the practice of medicine, are used to produce systemic changes.
2. Secrecy should be abolished regarding the ingredients of products offered to the public for cosmetic use. Complete knowledge of the chemistry and composition

158. Robertson, D. F., M.D., chemist, Merck & Co.: Personal communication to the authors.

159. M. C. Phillips (of Consumers' Research) Skin Deep, p. 117. Pub. Consumers' Research, Inc., Washington, New Jersey.

of such preparations should be readily available. It is well established that even small quantities of substances may cause an allergic response in certain individuals.

3. The widespread and uncontrolled use of therapeutic agents such as hormones and vitamins in cosmetics makes it necessary to determine their margin of safety and their efficacy if used in this manner.

4. Cosmetic preparations which function by hormone or vitamin action might more properly be classed as therapeutic agents.

745 Fifth Avenue.

Therapeutics

THE THERAPY OF THE COOK COUNTY HOSPITAL

EDITED BY BERNARD FANTUS, M.D.
CHICAGO

NOTE.—*In their elaboration, these articles are submitted to the members of the attending staff of the Cook County Hospital by the director of therapeutics, Dr. Bernard Fantus. The views expressed by various members are incorporated in the final draft for publication. The articles will be continued from time to time in these columns. When completed, the series will be published in book form.*—ED.

THE THERAPY OF ACUTE PERIPHERAL CIRCULATION FAILURE: SYNCOPE, SHOCK AND COLLAPSE

IN COLLABORATION WITH DR. LINDON SEED

Acute circulatory failure may be of three etiologic types: It may be due to heart failure (q. v.), to hemorrhage (q. v.) or to failure of the peripheral circulation. To distinguish between these types carefully is of practical therapeutic importance because digitalis bodies are likely to be of value in only certain of the cardiogenic types and may be harmful in others.

In the type due to hemorrhage, the filling of the depleted vessels is of prime importance and, when this is due to loss of blood volume, prompt blood transfusion is the remedy. In this condition vasoconstrictor drugs may do harm.

Failure of the peripheral circulation includes a number of clinical syndromes characterized by inadequacy of circulating blood volume (absolute or relative) due to causes other than hemorrhage. In traumatic shock there is practically always loss of blood, but this is insufficient in degree to cause the clinical picture.

The insufficiency of circulating blood volume results in a great decrease in venous return flow and hence of cardiac output, a fall in arterial and capillary pressure, a small pulse pressure and an anemic anoxia of all the organs, most significantly of the brain. The reflexes are decreased or abolished. The skin is ashy gray and is covered with cold perspiration. This failure of the peripheral circulation may be of most complex causation and is perhaps best discussed under the traditional clinical concepts of syncope, shock and collapse, provided these terms are given definite meanings, which they at present by no means enjoy. We shall here distinguish between syncope, traumatic shock and collapse.

SYNCOPE

Syncope, neurocirculatory failure, fainting or swooning is a sudden and, unless quickly fatal, transient form of general systemic depression, characterized by an unexpected, partial or complete suspension of consciousness and of locomotion and often of circulation and respiration.

Failure to maintain an adequate cerebral circulation is due to psychic or reflex (i. e. neural) influences affecting cardiac and vascular functions. This neurogenic collapse may be of several types: (1) vasovagal syncope, (2) vasal syncope, (3) cardiac syncope and (4) carotid sinus syncope.

All these types are characterized by their transient natures (unless the patient dies, which may happen) and by the absence of marked hemic or chemical changes.

1. *Vasovagal Syncope.*—This is the most common type. It is the ordinary "fainting spell" and is due to a combination of vasodilator and cardio-inhibitory actions which results in a greatly diminished return of blood to the heart. It occurs most commonly in predisposed persons suffering from vasomotor instability and a tendency to postural hypotension, which may be constitutional or acquired, as from prolonged bed rest, debilitating conditions such as fatigue, fasting, anemia or other disease. The precipitating factors, acting most especially by producing splanchnic vasodilatation, are prolonged standing in crowds, sudden getting up after prolonged recumbency, or the rapid withdrawal of large quantities of fluid (e. g. "tapping" of ascites). If under these conditions vagus stimulation occurs as the result of fright, pain or other profound emotion, the patient loses consciousness. Reflex stimulation from almost any instrumentation or from a blow on the solar plexus produces the same result. When the patient falls, the resultant low position of the head remedies the cerebral anoxemia and revival takes place, though the weakness continues for some time thereafter.

Diagnosis: The patient may fall in a faint without warning or the unconsciousness may be preceded by premonitory symptoms, such as epigastric or precordial distress, giddiness and light headedness, yawning, belching, nausea or abdominal or heart pain. The skin is ghastly pale, the veins are collapsed, the pulse is small or imperceptible, the pupils are dilated and the conjunctival reflex is absent. The heart sounds are slow and weak, the blood pressure is low, and the respiration is shallow and slow or deep and sighing. There may be clonic muscular movements. After a few seconds or minutes, sometimes right after involuntary urination or defecation, the pulse improves and consciousness returns, possibly with nausea and even vomiting, and usually with profuse perspiration. It is frequently followed by headache and weakness, which may last for some time. No other condition so nearly resembles death, and yet death occurs but rarely, as when, for one reason or another, sufficiently prompt recovery of an adequate cerebral or cardiac circulation is impossible, as when a patient collapses in a chair so that complete lowering of the head is prevented.

Prophylactic Therapy: Stability of the vasomotor system should be improved and anemia or any other systemic abnormality should be rectified. Ephedrine from 0.015 to 0.030 Gm. three times a day may be a preventive. An abdominal support may be of value. Instead of standing motionless for a long time the patient should shift the weight of the body from one leg to the other. After prolonged bed rest he should get up very slowly and should be watched especially during urination, defecation or emesis. Whenever premonitory symptoms appear he should lie down immediately. Fright or other emotion should not be permitted

Dr. Fantus died, April 14.

to aggravate the attack. During instrumentation of any kind the sitting posture should be avoided, especially by weak patients. Preoperative administration of sedatives and local anesthesia prevent syncope. Thus, prior to pleural operations the patient should receive from 0.10 to 0.20 Gm. of soluble phenobarbital and 1 mg. of atropine subcutaneously. Local anesthesia should be applied not only subcutaneously but also intrapleurally.

Treatment: Since, in contradistinction to the normal, the circulation in syncope is affected by gravity, the head-down or "shock" position should promptly be assumed and the legs elevated. The clothing should be loosened. Reflex stimulation may be secured by applying cold water to the face or by cautiously inhaling ammonia vapor, preferably from aromatic spirit of ammonia. Inhalation of oxygen with 10 per cent carbon dioxide may be helpful. Intravenous administration of 1 mg. of atropine sulfate or of 1 cc. of epinephrine in 1:10,000 solution may result in instantaneous recovery. In profound syncope subcutaneous injection is of no use because of poor absorption. Artificial respiration and heart and thoracic massage should be promptly resorted to if the condition seems desperate. The patient should be permitted to lie down until fully recovered. Against the consecutive headache one may use acetylsalicylic acid or another analgesic.

2. *Vasoconstrictor Syncope.* — This occurs from stimulation of the vasomotor center by chemical or mechanical agents. Most characteristic of this type is the syncope following administration of a local anesthetic in which the patient, usually sitting in the dentist's chair, collapses, may have convulsions and may even die.

The therapy is in many respects similar to that of the vasovagal type. The administration of barbiturate is prophylactic and the slow intravenous injection of soluble phenobarbital (0.50 Gm.) may be life saving during an attack. Administration of epinephrine is contraindicated in this condition.

3. *Cardiac Syncope.*—The cardiac type of syncope occurs whenever the output from the heart is insufficient to maintain an adequate blood supply to the brain. It may be vagal syncope, which occurs typically in the Adams-Stokes syndrome: "syncope plus slow pulse" sometimes accompanied by convulsive seizures. This vagal syncope may be due to organic heart disease with auriculoventricular block (true Adams-Stokes disease) or be of reflex origin. Cardiac syncope also may occur in paroxysmal tachycardia as well as in angina pectoris and in congestive heart failure, i. e. whenever the heart output suddenly becomes inadequate to maintain sufficient cerebral circulatory activity. As these conditions are instances of "heart failure," their treatment will be discussed under this heading.

4. *Carotid Sinus Syncope.*—This type may be vasal or vagal. The function of the carotid sinus (a bulbous dilatation rich in sensory nerves located at the bifurcation of the internal carotid artery) is to prevent undue rise of arterial pressure and excessive increase of heart rate. Its stimulation results in cardio-inhibition and/or vasodilatation. Hypersensitiveness of the carotid sinus or organic lesions in its vicinity may result in spontaneous syncope, attacks of which may be induced in such cases by pressure on the carotid sinus, which is pathognomonic of such hypersensitiveness. There are three varieties of carotid sinus and syncope: one in which the pulse is markedly slowed, a second in which the blood pressure drops profoundly and a third in which convulsions are produced.

In addition to placing the patient in the horizontal position and loosening the clothing, particularly around the neck, the administration of epinephrine is indicated. Atropine is especially useful if the pulse is markedly slowed. For the prevention of attacks, atropine sulfate in 0.5 mg. doses two or three times a day may be beneficial or, if this fails, ephedrine in from 15 to 30 mg. doses may sufficiently increase the irritability of the myocardium to prevent the slowing of the heart rate. In otherwise unmanageable cases, surgical section of the nerve or denervation of the sinus is justified.

TRAUMATIC SHOCK

Traumatic shock, as it is seen in hospitals, should be defined as a depression of the vital processes consequent on severe physical injury and due to a great insufficiency in volume of circulating blood, which may be partly due to actual loss of blood to the exterior into some of the body cavities or into the soft tissues and partly or entirely due to "plasmosis," i. e. exudation of blood plasma into the injured area. This is what is commonly called "secondary shock." What is called "primary shock" is syncope, being characterized by suddenness of onset and a tendency to recovery (reaction), especially in the head-low posture. Shock may insensibly pass into vasodilatation collapse (q. v.).

Diagnosis.—From a clinical point of view, the most important definite factor in the diagnosis and treatment of traumatic shock is the low blood pressure. The diagnosis of shock cannot be made without a low blood pressure, and the degree of drop in the blood pressure roughly corresponds to the degree of shock. Not only does the low blood pressure often precede the other clinical manifestations but its drop determines also the quantity of fluids to be administered. One continues treatment governed largely by the effect of the treatment on the blood pressure. From a practical point of view, for instance, one could say that if the systolic blood pressure is under 90 the patient is unlikely to survive a major operation.

The Stages of Shock.—The so-called primary shock is essentially syncope. It is more severe in adults than in children and in nervous than in phlegmatic persons, and is also severe in persons crippled by organic disease; it is more prone to occur under the influence of hunger, fatigue, exposure, fear and terror. Owing to the importance of the psychic element, the degree of shock may be proportionate even to the patient's idea of the gravity of his condition, whether the actual damage is really great or the patient merely thinks it so. The more sensitive the tissue damaged the more nerves are involved in the injury, or the larger the nerve injured the greater is the degree of shock. This is the reflex (syncopal) factor.

The "reaction" stage usually sets in within a few hours if the condition is not speedily fatal. The reaction is possibly due to a number of influences: the waning of the syncopal factor, or the vasopressor action of accumulating carbon dioxide and of adrenal secretion. Marked delay in the onset of the reaction should cause one to look for complicating hemorrhage (q. v.), hemoconcentration collapse (discussed later), or acidosis (q. v.). The reaction sets in with the return of color to the face, the pulse becomes slower and stronger and the temperature rises, sometimes above normal. Vomiting may usher in the reaction. If vomiting occurs during the first stage, it is a bad omen.

The stage of "secondary shock" may supervene on the reaction or on alternate periods of reaction and

depression. The secondary shock is usually due to hemorrhage and/or exudation. In either case the reduction in the volume of circulating fluid results in stimulation of the vasomotor center, so as to maintain a degree of circulatory activity compatible with life. Under these circumstances the vasomotor center keeps, by splanchnic vasoconstriction, the blood pressure higher than it would otherwise be. If in spite of this the blood volume continues to fall, the condition passes insensibly into "vasodilatation" collapse from failure of the vasomotor center due to inadequate blood supply, and now the splanchnic blood vessels dilate. When this occurs, and especially when in addition these vessels have become leaky as a result of prolonged impairment of their nutrition, the condition is fatal, responding to no therapeutic efforts. The practical lessons to be drawn from these considerations are, first, that for a patient in shock, as also for the patient in hemorrhage, general or subarachnoid anesthesia is extremely dangerous because of their vasodilator tendencies. Secondly, promptness is an essential factor to success in treatment. If the correct treatment is not applied at the right time, no amount or kind of treatment will do any good.

The symptoms of shock may be described as follows:

The patient, after an automobile accident, is brought into the hospital on a stretcher. He is moaning gently, seems restless and has little interest in his surroundings. His respirations are a bit hurried; his forehead is pallid, slightly wrinkled and covered with fine drops of cold sweat. His eyes are a shiny white; the nose is pinched and has a bluish tinge. The lips are purplish gray. There is written on his face not only the anguish of pain but the fear of impending dissolution. His hands lie powerless at his side; the finger nails are the color of an overcast sky. The hand is covered with a cold and clammy dew. The radial pulse is merely a flicker in the wrist and it can be counted only with difficulty at 120 to 130 to the minute. When the blood pressure is taken the first beats come through at 85 mm. and fade out at 70 mm. The thermometer inserted in the rectum registers 96 F. When he is moved from the stretcher into bed, the bones of the pelvis can be felt to rasp one against the other. He does not cry aloud but moans softly. Even if no treatment is instituted, in an hour or two he seems improved and asks concerning his friends who were in the wreck. Merciful nature has stopped all sensation of pain, but the flicker that was in his wrist is gone. When the blood pressure is taken one can hear at 60 mm. beating as of the hoof beats of a horse as his rider drives him far across the prairie and into the horizon. Soon, and rather quietly, he falls asleep, his respirations become irregular, now fast, now slow and finally cease.

Prophylactic Therapy.—Operation shock, like sepsis, is more easily prevented than treated once it has occurred. It is the debilitated patient who is the most likely to have operation shock. A debilitated patient is one who has a loss of strength or loss of weight or anemia or all three. These are the three most important criteria of tendency to shock.

1. Proper preparation of the patient tends to secure optimal resistance and reserve. Thorough preoperative examination of the patient with particular reference to the kidneys and elimination (routine examination should include the amount of voided urine and the amount of chloride in twenty-four hours). Excepting in an emergency, no patient should be sent to the operating room who has not passed at least 1,000 cc. of urine in the preceding twenty-four hours and whose urine is not free from sugar and diacetic acid and does not contain at least 0.3 per cent sodium chloride. Whenever a patient cannot thus be prepared for operation this fact should be prominently noted, as such patients require special after-care. Prolonged starvation before operation should be avoided and sleeplessness prevented the night before operation by administration of a suitable hypnotic, if required. The night must not be made hideous by preparation for the operation if it can possibly be avoided. Blood should be examined for alkali reserve and sugar. If the operation cannot be postponed, in the presence of acidosis, the operation should be preceded by intravenous injection of dextrose solution (see also Acidosis). In the presence of severe anemia, it is imperative to give a preoperative blood transfusion. Purgation before operation is no longer resorted to. If required, an evacuant enema is employed.

2. Expert anesthesia minimizes the causative reflex factor. In some cases morphine 8 to 10 mg. and scopolamine hydrobromide 0.5 mg. hypodermically twenty minutes before operation are useful to combat restlessness and lessen the amount of anesthetic required. The duration of the anesthesia should be as short as possible. In the presence of shock a local anesthetic is best. Next comes ethylene, and ether comes last in order. During the period of anesthesia it is imperative that an accurate check be made on the blood pressure and pulse rate.

3. Tissue trauma increases shock by increasing the amount of "exudation": hence tissue trauma must be minimized; so must nerve injury. Operations should be performed as expeditiously as possible and handling, exposure or injury of the tissues reduced to a minimum. Careful prevention of loss of blood is also essential.

4. Psychic shock should be prevented by reassuring, kindly and humane treatment of the patient, by avoiding delay in operation as well as by not permitting anything to occur that may frighten him.

5. Bodily warmth should be maintained, the exposure being avoided, and there should be no delay in returning the patient to bed from the operating room.

6. A patient in shock with a systolic blood pressure under 90 should never be operated on unless a continuous blood transfusion is being given during the operation. A continuous transfusion of blood during operation may allow one to do an imperative operation safely on a patient in severe shock.

Treatment.—1. Absolute rest should be secured and pain and distress relieved. Morphine hypodermically (0.02 Gm.) or, if injection is impossible, sublingually (crushed hypodermic tablet under the tip of the tongue) to cut off the psychic influences that aggravate shock is considered the single most important medicine for the patient in shock. Alcohol (whisky or brandy) acts similarly and may be given by mouth or, if swallowing is impossible, diluted with hot water by rectum, provided it is certain that there is no perforation of an abdominal organ. Fear and despair should be allayed by a kindly and reassuring manner. A single tactless remark may turn the tide against the patient. The inflow of sensory stimuli from the site of the injury should be minimized by splinting or otherwise preventing damage to the nerves. Rough and prolonged transportation and delayed treatment of the wounded, as in battle, greatly aggravate shock. Until reaction has set in, manipulation of the injured part should be restricted to that demanded for the checking of hemorrhage and the minimizing of pain and distress.

2. Body heat must be maintained. The tendency to subnormal temperature causes a vicious circle, because

there is no greater depressant to vital function than a subnormal temperature. In its presence, stimulants fail to act. Heat may be applied by an electric light bath, hot blankets, hot bricks or bottles filled with hot water; but great care should be exercised against burning the patient, for when the circulation is poor tissue is easily damaged by heat. If the temperature is quite low, the quickest way of restoring it is by a hot bath or a hot wet pack, for dry heat penetrates but slowly and poorly. One may pour hot water (avoid scalding!) over the clothing of a person to be resuscitated after drowning. Exposure to cold and wet greatly aggravates subnormal temperature and shock. Hot drinks, hot enemas and hot infusions are helpful. Diathermy is advocated.

3. Blood circulation should be maintained in the vital parts of the body by having the head on a level with the body or lower than the feet, provided this does not cause cyanosis and there is no head injury. In any severe case autotransfusion (bandaging limbs after raising each in turn for a few minutes) may be of value. If hemorrhage is present, it must be arrested as soon as possible and the loss of blood made good by a blood transfusion as promptly and as thoroughly as the occasion permits.

Lost body fluid should be restored. In all cases of severe shock, the pulse and blood pressure should be observed at frequent intervals (most reliable indicator of severity of shock): also a complete blood count should be made, followed by repeated red blood cell counts and hemoglobin estimations. Whenever blood in considerable amount has been lost and the blood count is low, blood transfusion is the supreme and may be life-saving remedy. Even if no blood has been lost it is still the best fluid, because it stays in the leaky vessels. If human blood cannot be procured, acacia solution (6 per cent acacia in 0.7 per cent salt solution) is probably the best substitute, as this does not leave the vessels as quickly as salt solution. Dextrose solution is somewhat superior to physiologic solution of sodium chloride, as dextrose remains in the blood vessels somewhat longer than does salt, and previous deprivation of nourishment or the presence of acidosis is relieved by the addition of the dextrose. As this sugar must be used in quantity to do any good, the percentage to be used depends on the amount of fluid that can safely be infused under the existing conditions of heart weakness. If the heart is very weak, 25 cc. of 50 per cent dextrose solution may be best. If 1,000 cc. can safely be injected, a 5 or 10 per cent solution will suffice. Fluids used in shock should be given as hot as can be borne (about 110 F. intravenously, not subcutaneously). These fluids given intravenously must be administered very slowly drop by drop and stopped as soon as some improvement has been secured, for giving too much fluid or giving it too rapidly may seriously embarrass the right side of the heart.

Unfortunately all these measures are merely symptomatic, as they do not relieve the underlying cause—the loss of peripheral vascular tone. In profound shock the administration of fluid by hypodermoclysis is relatively futile, because in this condition fluid passes out of the capillaries and, in the presence of shock severe enough to be fatal, fluid thus given is not likely to be absorbed. By mouth only small quantities of water are admissible, otherwise attempts to quench the shocked patient's thirst leads to vomiting. Water absorption from the stomach is nil.

4. Circulatory stimulants are important. The only drug that may be of any value in the final (vasodilatation) stage of collapse is epinephrine; but unfortunately its effect is so transient—lasting but a few minutes—that it is of value only as a temporary measure to give time for the administration of more valuable measures, such as transfusion. It must be administered intravenously. It is useless when given by mouth or hypodermically. It is best given very slowly in 1 cc. doses of the 1:10,000 dilution. During phleboclysis a 1 cc. dose of this dilution may be added from time to time by puncturing the previously sterilized rubber tubing of the infusion apparatus. Epinephrine should be infused very slowly, at just the rate to maintain blood pressure at a safe level, for the effect of epinephrine is just as fleeting as it is prompt. In extreme emergency, intraauricular injection of epinephrine 1 to 5 cc. of 1:1,000 solution may possibly be life saving.

In the presence of distention of the bowel, pitressin (1 cc.) may be a valuable addition. It must be given intramuscularly, as no drug is likely to be of any value when administered hypodermically in cases of severe shock, for it will probably not be absorbed until the emergency is over. If facilities for infusion of the vein are not at hand, intramuscular injection of epinephrine solution (1 cc. of 1:1,000) may be employed, with the hope that the inhalation or oral administration of a reflex stimulant such as aromatic spirit of ammonia or the ingestion or rectal administration of whisky or brandy, diluted with hot water, may give a sufficient stimulus to the circulation to permit absorption of the other stimulant. The stimulation must not be overdone for fear of starting up hemorrhage. Strong liquor should not be poured down a shocked person's throat—he may not be able to swallow properly and aspirate it into the larynx, which may aggravate the shock. Strychnine or other stimulants that increase reflex activity should be tabu in shock, for shock is increased by reflex excitation.

COLLAPSE

Collapse is a condition of extreme prostration due to (1) absolute or (2) relative insufficiency of blood volume without actual loss of blood. It is of slower onset than syncope or shock and of indefinite duration.

Forms.—1. Collapse due to absolute insufficiency of circulating fluid occurs from (*a*) exsiccosis, i. e. insufficient intake of fluid, (*b*) hypochloridemia, excessive loss of salt and fluid (vomiting, sweating) or (*c*) "plasmosis," i. e. excessive loss of blood colloid due to leakiness of blood vessels. The term "serous inflammation"[1] has been proposed for this condition of damage to the vascular endothelium from tissue destruction products, whether caused by a burn, freezing, corrosion or trauma, resulting in a leakage of plasma through the capillaries. As none of the other evidences of inflammation (excepting this leakiness of vascular endothelium) are in evidence, the term "plasmosis" is proposed as possibly more appropriate. This condition, probably due to tissue disintegration products, is liable to set in whenever circulation is seriously interfered with in any vascular territory.

2. Relative insufficiency of circulating fluid may occur from:

(*a*) Depression of the vasomotor center, from poisoning by drugs, most especially those of the aromatic series, e. g. phenol and the antipyretics.

(*b*) Degenerative changes in vascular tissue due to toxins of infectious diseases. This condition is frequently spoken of as "heart failure," but actually the vasodilatation is in the center of the picture. The

1. Serböse entzündung, Eppinger and Popper.

symptom complex of true heart failure (q. v.) includes dyspnea, more marked cyanosis and a tendency to edema, pulmonary or systemic.

(*c*) Collapse, which may be due to functional impairment or degeneration of endocrine glands, such as the adrenal or pituitary.

3. Combinations of these two forms of collapse (1 and 2) occurring in various ways and degrees may make the clinical picture exceedingly complex.

Diagnosis.—This skin is pale and cold (even if there is fever) and clammy, and it may be grayish (owing to cyanosis, especially of the lips, nose, fingers and toes); the face appears pinched, and the nose prominent. The pulse is rapid and feeble, the blood pressure and pulse pressure are low. There is great diminution or even cessation of urinary secretion. The temperature may be subnormal or rise very high in febrile collapse. There is muscular weakness and relaxation. Mental depression and apathy are present, but consciousness is preserved until near the end. When delirium and coma set in, death is usually near.

Prophylactic Therapy.—This is of greatest importance, as treatment is often futile once advanced collapse is present. Therefore every possible effort must be made to discover early the tendency to collapse and to treat correctly the underlying condition, whether this is infection, intoxication, systemic hypohydration, chloride deficiency or plasmosis.

Treatment.—1. Absolute rest is indicated with the head low to keep the blood in the vital centers. "Autotransfusion" by elevation and centripetal bandaging of the limbs and compression of the abdomen may be tried. Should cyanosis set in, however, this may be held as evidence that these maneuvers are being overdone—that the heart is being embarrassed by them.

2. Hot stimulating drinks (coffee or tea), if the patient can swallow, should be given in small quantities frequently repeated. No food requiring digestion should be administered until the crisis has passed; nor should large quantities of fluid be given by mouth.

3. If the body temperature is subnormal, external heat is the single most important stimulant. While the hot bath is most efficient, an electric light bath under "cradled" bed clothes is next best, if the patient should not be subjected to the strain of the bath. The use of hot water bags or bottles carries with it the danger of inducing burns if they happen to be placed too close to the skin; and burns occur in the collapsed patient much more readily than in one whose circulation is more adequate. In febrile collapse (internal temperature high, skin pale), bringing the blood to the skin by hot sponging or a mustard bath or mustard pack followed by a brief cool procedure, to "fix" the blood in the skin, is the method of choice.

4. Fluid of some sort must be administered, and usually parenterally, as absorption from the gastrointestinal tract is very poor.

(*a*) If the condition is serious, blood transfusion should be employed and repeated as required. This is much superior to infusion of acacia solution.

(*b*) If there is exsiccosis (merely water deficiency) 2.5 per cent dextrose in half strength (0.45 per cent) normal salt solution is perhaps the best infusion fluid, given hot (110 F.) if the temperature is subnormal. If the heart is feeble, only small quantities at a time are admissible, preferably given by intravenous drip. If required, it may be given continuously (preferably by tandem flask) and 3,000 cc. introduced in the twenty-four hours. In hypohydration collapse the administration of colloid fluid is inadvisable, as it tends to prevent the fluid from reaching the tissues, where it is needed.

(*c*) In hypochloridemia collapse, phleboclysis of hypertonic (10 per cent) sodium chloride solution (10 to 20 cc.) should precede other therapy.

(*d*) Hypodermoclysis of 5 per cent dextrose may be considered in less serious conditions. This must not be given at much above 100 F. for fear of producing sloughs.

(*e*) Rectal injection of hot fluid (120 F.), preferably hot black coffee, is to be considered in mild collapse.

5. The abnormal chemistry of the tissue fluids should be corrected. Disturbance of the acid-base balance of the system, either acidosis (q. v.) or alkalosis (q. v.), should be taken care of in connection with the introduction of fluids, as indicated.

6. Correction of disturbed circulatory mechanics is usually spoken of as "stimulation." An estimate should be made of the relative participation of the heart, the blood vessels, the endocrines and the nervous system in the existing depression of the circulation:

(*a*) Epinephrine (from 0.5 to 0.75 cc. of 1:1,000 solution) administered extremely slowly, preferably much diluted, in intravenous drip may be of telling effect, especially if there is peripheral vasoparesis, particularly if this is due to endocrine deficiency. Epinephrine is contraindicated if there is a tendency to pulmonary edema.

(*b*) So-called diffusible stimulants, aromatic spirit of ammonia, or whisky or brandy, may be given by mouth or in hot black coffee by rectum. The effect of these should be carefully noted; they should not be repeated unless they produce at least temporary improvement.

(*c*) Inhalation of amyl nitrite (0.30 cc.) may bring a flush to the face and improve conditions if spasm of the cerebral capillaries is present; but, in general, nitrite must be avoided whenever there is great diminution in the volume of circulating fluid.

(*d*) Atropine sulfate (1 mg.) by hypodermic injection may be especially useful in collapse with "leaky" skin. When it is used, improvement in the circulation must be judged by the increased vascularity of the skin rather than by slowing of the pulse, as atropine sulfate may accelerate the heart beat while improving the circulatory condition.

(*e*) Strychnine sulfate, in a great emergency, possibly in doses as high as 3 mg. given intramuscularly, is too well established clinically as an available stimulant to be discarded on the basis of negative results in experiments on healthy animals. It may possibly act indirectly by stimulating adrenal secretion.

(*f*) Caffeine with sodium benzoate (0.5 Gm. ampule) given intramuscularly may be of value, especially if there is cerebral depression.

7. Camphor (in oil) 1 cc. intramuscularly and repeated at intervals once or twice a day was formerly a popular stimulant. Metrazol (1 to 3 cc.), which is similar but more prompt in action, has largely replaced it.

8. Digitalis bodies, preferably strophanthin (if digitalis has not been given for days previously) in doses of from 0.25 to 0.5 mg. in 10 per cent dextrose solution intravenously should be used if there are indications of myocardial failure. If it improves conditions, this should be followed by administration of digitalis by mouth.

The redundancy of the remedies offered does not mean wealth but rather poverty in reliable measures: it

does not mean knowledge but ignorance of specific remedies. These various agents should not be piled on indiscriminately. The effect of any one of them should be carefully noted before repetition of the dose, for they may harm as well as help. Plying the dying with "stimulants" is nothing less than inhumane.

9. The respiratory conditions should be improved. If cyanosis supervenes, oxygen inhalation, possibly with 5 per cent carbon dioxide to act as a respiratory stimulant, may be employed; but it should not be used as a routine before death because it adds to the discomforts of the dying and, besides, it would be a waste of expensive gas. To be of value it must used early; it should be remembered that collapsed patients become gray from cyanosis rather than blue. Artificial respiration may be resorted to in an acute emergency if breathing becomes enfeebled or irregular.

10. When a patient who has been in collapse rallies he is in need of prolonged rest in bed and careful "building up" treatment, as the damage to the circulation is likely to be recovered from very gradually.

Council on Pharmacy and Chemistry

REPORT OF THE COUNCIL

THE BOARD OF TRUSTEES REQUESTED THE COUNCIL ON PHARMACY AND CHEMISTRY TO MAKE A STUDY OF THE PROMISCUOUS USE OF BARBITURATES, PARTICULARLY WITH REFERENCE TO THE DANGEROUS USE OF THESE PRODUCTS BY THE PUBLIC. THE REPORT HAS BEEN DRAWN UP IN TWO SECTIONS. THE FIRST SECTION, ENTITLED "A STUDY OF THE PROMISCUOUS USE OF THE BARBITURATES: THEIR USE IN SUICIDES," WAS PUBLISHED IN THE JOURNAL, APRIL 8, 1939, p. 1340. THE COUNCIL HAS CONSIDERED THE SECOND REPORT, ENTITLED "THE PROMISCUOUS USE OF THE BARBITURATES: II. ANALYSIS OF HOSPITAL DATA," AND AUTHORIZED ITS PUBLICATION, AT THE SAME TIME AGAIN EXPRESSING APPRECIATION TO DR. HAMBOURGER FOR HIS EXCELLENT COOPERATION.

PAUL NICHOLAS LEECH, Secretary.

THE PROMISCUOUS USE OF THE BARBITURATES

II. ANALYSIS OF HOSPITAL DATA

W. E. HAMBOURGER, PH.D., M.D.

CLEVELAND

In a previous communication [1] a survey was made of coroners' records of suicidal deaths due to barbiturates. The present report deals with the involvement of these drugs in cases of poisoning received at hospitals during the decade 1928-1937. The data were obtained from fifteen hospitals in reply to a questionnaire. Additional data were added from the medical literature. The hospitals which volunteered the requested information and their officials are as follows:

Baltimore: City Hospital, P. J. McMillin, superintendent; Johns Hopkins Hospital, E. L. Crosby, M.D., statistician and supervisor of records.

Boston: City Hospital, C. H. Pelton, M.D., assistant superintendent; Peter Bent Brigham Hospital, E. C. Cutler, M.D., surgeon-in-chief.

Chicago: Presbyterian Hospital, E. E. Irons, M.D.; Michael Reese Hospital, Record Room; University Clinics, N. Gorgas, assistant to the director.

Cleveland: Cleveland City Hospital, G. P. Bugbee, superintendent; University Hospitals, J. M. Hayman Jr., M.D.

Dallas, Texas: Baylor University Hospital, G. M. Hilliard, M.D., acting medical director.

New York: Presbyterian Hospital, W. H. McCurdie, assistant superintendent.

St. Louis: St. Mary's Hospital, Sister Mary Servatia, S.S.M., medical record librarian.

Washington, D. C.: Walter Reed General Hospital, J. L. Murchison, M.D., Captain, Medical Corps, Adjutant.

The following two hospitals have been omitted from this summary because they did not report any cases of intoxication by barbiturates:

Alms House Hospital, Newark, N. J., F. W. Becker, M.D.
Quincy City Hospital, Quincy, Mass., J. P. Leone, M.D.

It will be noted that the thirteen hospitals whose data are analyzed in the present study are located in larger cities in the New England, Atlantic, Middle Western and Southwestern areas. Hospitals in other parts of the country failed to supply information. Although this distribution does not represent a typical cross section of American life, nevertheless the statistics available for study represent more than one and one fourth million hospital admissions for the decade 1928-1937. A few of the hospitals did not furnish information on the total number of admissions for all causes and for all types of poisoning cases. This made it necessary when determining percentage values to omit their data from the calculations.

The data will be discussed under the headings of (1) acute intoxication, (2) hypersusceptibility, (3) addiction and (4) chronic poisoning.

ACUTE INTOXICATION

The thirteen hospitals which supplied the data (table 1) reported a total of 643 cases of poisoning by barbiturates during the decade 1928-1937. Of these, forty-seven cases, or 7.3 per cent, were fatal. During the decade, ten of the hospitals received 555 cases of barbiturate poisoning among 3,936 cases of poisoning by all drugs (except carbon monoxide and alcohol). Barbiturates, therefore, represented about one seventh, or 14.1 per cent, of all the poisonings. Twelve of the hospitals had a total of 1,254,465 admissions for all causes during this interval, of which barbiturates made 0.053 per cent, or about one case in every 1,900.

As in the previous communication, which analyzed successful suicides,[1] the incidence of involvement of barbiturates in the cases of poisoning received by the hospitals varied widely in different localities. The range is from 5 per cent at Baylor University and New York Presbyterian hospitals to 20 per cent at Michael Reese Hospital in Chicago. But unlike the distribution of suicides, the ratio of barbiturate poisoning to all drug poisonings is quite variable, even within a given locality. For instance, in contrast to Michael Reese Hospital in Chicago, where the incidence was 20 per cent, it was only 9 per cent at the University of Chicago Clinics. In Baltimore it was 18.5 per cent at the Johns Hopkins Hospital (1936 and 1937 only) while it was 2.6 per cent at the City Hospital (1935-1937 only). Presumably the reason for such variations lies in the different clienteles of the institutions, the relative percentage of emergency cases, surgical cases, and so on.

Somewhat better correlation as to locality can be observed when admissions for barbiturate poisoning are compared with admissions for all causes. These values are given in table 1 in the order of descending ratio.

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An article on the legal aspects of the subject of the promiscuous use of barbiturates, prepared by the Bureau of Legal Medicine of the American Medical Association, appears in this issue, page 2029.

1. Hambourger, W. E.: A Study of the Promiscuous Use of the Barbiturates: Their Use in Suicides, J. A. M. A. **112**: 1340 (April 8) 1939.

On this basis the frequency of poisoning by barbiturates is highest in the New England area, intermediate in the Middle West and lowest in New York City and the Southern areas.

The relative occurrence of accidental barbiturate poisoning as compared with suicidal poisoning also varies considerably in the reports from the different hospitals. Four classifications could be recognized: (1) definitely suicidal, (2) probably suicidal, (3) probably accidental and (4) definitely accidental. There was no uniformity in the reports, presumably because of the difficulty in obtaining a truthful or accurate history from a patient in coma or from his distraught relatives.

The total reported as definite accidents (309) was greater than the total reported as definite suicides (193), but in six reports there were more suicides than accidents. There were also twice as many probable accidents (ninety-eight) as probable suicides

TABLE 1.—*Acute Poisoning by Barbiturates*

Hospital*	Hospital Admission All Causes (A)	Poisoning Cases Excluding CO and Alcohol (P)	Barbiturate Poisoning (B)	Percentage of All Poisoning Cases B — 100 P	Percentage of All Admissions B — 100 A
Boston City	331,481	2,214	391	17.7	0.118
Peter Bent Brigham, Boston	43,885	214	26	12.1	0.059
Cleveland City	129,983	†	60	....	0.046
University Clinics, Chicago (Oct. 3, 1927, to October 1938)	63,076	117	18	15.4	0.028
University Hospitals, Cleveland	91,703	245	23	9.4	0.025
St. Mary's, St. Louis	75,024	99	18	18.2	0.024
Michael Reese, Chicago	142,067	169	34	20.1	0.024
Presbyterian, New York	135,352	444	22	5.0	0.016
Johns Hopkins, Baltimore (1936-1937 only)	32,703	27	5	18.5	0.015
Baylor University, Dallas, Texas	109,138	293	15	5.1	0.014
Baltimore City (1935-6-7 only)	25,356	114	3	2.6	0.012
Walter Reed General, Washington, D. C.	74,067	†	7	....	0.009
Presbyterian, Chicago	†	†	21	....	.....
Totals					
Twelve hospitals excluding Chicago Presbyterian	1,254,465	.....	622	....	0.049
Ten hospitals excluding Cleveland City, Walter Reed General, and Chicago Presbyterian	1,050,415	3,936	555	14.1	0.053

* 1928-1937 inclusive except as noted.
† Not reported.

(forty-three). It seems likely that many cases labeled as accidents were really attempted suicides, patients and relatives disguising the intent of the poisoning. Twenty-three of the cases reported as definite suicidal attempts were fatal; so also were eight of the probable suicides. Ten definite accidental and seven probable accidental poisonings were likewise fatal. No definite correlation between etiologic category and size of fatal dose was apparent. The incidence of fatality, however, was distinctly higher for the suicides than for the accidents. There were thirty-one deaths from 236 combined suicidal attempts, or 13.1 per cent, but only seventeen deaths from 407 cases of accidental administration, or 4.2 per cent.

The most frequently used barbiturates were barbital and phenobarbital, or their soluble salts, often in proprietary form. Presumably, since they are the oldest and, therefore, longest publicized members of the group, they are also the best known. The hospital reports clearly show a tendency for each new barbituric acid derivative to be involved in poisoning as soon as it becomes popularized; viz., amytal. Nearly every barbiturate which has received clinical trial was used in one or more cases of poisoning in the present series. Specifically ten barbiturates were used: barbital 360 times, phenobarbital 121, amytal fifty-eight, alurate five, ipral three, pentobarbital three, ortal two and dial, phanodorn and seconal one each. Also nine mixtures of drugs were used, seven of two or more barbiturates and two of a barbiturate with aminopyrine. Allonal, of the latter type, was involved in forty-eight cases of poisoning. Whenever these drugs or any other barbiturates are mentioned, the simple drug name is understood to include the sodium salt and any proprietaries.

Fatal Dosages.—The data of the thirteen hospitals permit comparison of fatal and nonfatal dosages. Table 2 lists the minimum, maximum and median fatal and nonfatal doses of the barbiturates most frequently involved in the 643 cases of poisoning. Doses were obtainable for only ten of the thirty-one cases of lethal poisoning by barbital. These were distributed quite uniformly from 30 grains to 360 grains, the median dose being 90 grains. A smaller dose (20 grains) was reported to have caused fatality in a chronic user. The nonfatal doses of barbital range up to 500 grains with a median value of 50 grains, a little more than half the median dose of the fatal cases.

Doses were reported for six of the nine deaths due to phenobarbital. They are distributed from 25 grains to 280 grains with a median dose of 142 grains. In one authenticated case a woman succumbed to 7½ grains, but the medical examiner's findings were: "Terminal edema of the brain following phenobarbital overdose. Cancer of the uterus." The extent of the carcinoma being unknown, it seems advisable not to count this as a case of phenobarbital poisoning. The maximum nonfatal dose of phenobarbital (140 grains) is nearly identical with the median dose in fatal cases of poisoning by the drug.

In a monograph on the misuse of hypnotics, Pohlisch and Panse [2] reported a series of fatal and nonfatal cases of poisoning by barbiturates which occurred in Germany between 1925 and 1932 inclusive. These have been tabulated with regard to dosage in table 3. The discrepancies between their figures and those in table 2 seem quite marked; but considering the shortcomings inherent in clinical histories and the resulting paucity of definite data, the fatal doses may well be accepted as being of the same order of magnitude. Pohlisch and Panse consider 4.5 Gm. (68 grains) the lower level of the danger zone for barbital, and doses of 10 Gm. (150 grains) or more as usually fatal. In the present hospital series the lower level of fatality is 30 grains, while doses above 90 grains are likely to be fatal. Leschke [3] reported ten deaths (about 7.6 per cent) in a series of 131 cases of phenobarbital poisoning. He gives the mortality rate in barbital poisoning as nearly 25 per cent. The variations in the fatality figures in the different collections of statistics are probably due largely to the obvious difficulties involved in obtaining accurate clinical histories. Final evaluation of the fatal and nonfatal dosage limits of the barbiturates does not seem possible until more data have accumulated in the literature.

2. Pohlisch, K., and Panse, F.: Schlafmittel-Missbrauch, Leipzig, Georg Thieme, 1934.

3. Leschke, E.: Die wichtigsten Vergiftungen, Munich, J. F. Lehmann Verlag, 1933, p. 165 (obtained from Report of the Council on Pharmacy and Chemistry: Present Status of Picrotoxin in Poisoning by Barbiturates, J. A. M. A. **112**: 431 (Feb. 4) 1939).

Mental Status.—The hospital questionnaires did not give specific information regarding the mental characteristics of the patients, but Pohlisch and Panse [4] charted the mental status in 707 cases of acute barbiturate poisoning. These are given, slightly modified, in table 4. It will be observed that a negligible number of patients were considered mentally "normal" and that the majority were of the psychopathic personality type. Only 6 per cent were epileptics.

HYPERSUSCEPTIBILITY

The thirteen hospitals reported a total of thirteen cases of toxic response to one, or relatively few, therapeutic doses of barbiturates, during the decade 1928-1937. These cases all came from six of the hospitals. Two cases from two other clinics were discarded as being chronic poisoning rather than hypersusceptibility. Three hospitals stated they had not received any such cases, and the remaining two failed to make any statement. On the basis of the hospitals which made a statement, the incidence of hypersusceptibility was about one case for every 90,000 admissions.

Data with regard to frequency of use were obtained on sixty-one of the barbiturate addicts. Two thirds of these (forty-two patients) took their drug daily, about one fourth (sixteen) used it occasionally, often for a "spree," and three were "frequent" users.

On admission to the hospitals, more than a third of the addicts (thirty-one) were in various stages of narcosis, presumably due to a superimposed acute barbiturate poisoning. In another third of the cases (thirty-one) no signs or symptoms of addiction were apparent or recorded, these patients presumably entering for some other reason. The remainder had various symptoms on admission, many showing signs of confusion.

Six of the addicts died from acute overdosage of barbiturate; five of them took it intentionally for suicide, and one death was reported as accidental.

When the barbiturates were withdrawn in the hospital, craving was recorded for twelve patients of the forty for whom data are available. Only one was reported to have had "withdrawal symptoms," which, however, were not described in detail. One patient complained of insomnia, another of nervousness and two of dizziness. In twenty-two cases no apparent withdrawal phenomena were noted. These facts agree with the generally accepted opinion that barbiturates do not produce withdrawal symptoms in the sense that such symptoms occur in opiate addicts.[5] Nevertheless, craving for the drug to the extent of continued use "in spite of strong medical advice to the contrary" is said to occur following daily therapeutic administration.[6]

TABLE 2.—*Comparison of Fatal and Nonfatal Dosages in 643 Cases of Acute Poisoning with Barbiturates in Hospitals in the United States (1928-1937)*

Drug	No. of Cases	Fatal Cases		Fatal Doses				Nonfatal Doses			
		No.	%	Number with Known Dose	Minimum	Median	Maximum	Number with Known Dose	Minimum	Median	Maximum
Barbital[a]	360	31	8.6	10	30 grains	90 grains	360 grains	197	5 grains	50 grains	500 grains
Phenobarbital	121	9	6.6	6	25 grains	142 grains	280 grains	60	3 grains	26 grains	140 grains
Amytal	58	3	5.2	1	.....	25 grains	.....	36	3 grains	25 grains	108 grains
Allonal[a]	48	2	4.2	1	.....	50 tablets	.....	32	4 tablets	12 tablets	60 tablets
Alurate	..	..	...	..	.....	50 grains	.....		4 grains	12 grains	60 grains
(Aminopyrine)	..	..	...	..	.....	(83 grains)	.....		(7 grains)	(20 grains)	(100 grains)
Alurate	5	1	20.0	1	.....	16 grains	.....	1	.....	24 grains	
Pentobarbital	3	0	0.0	0	.....	.....	.....	3	12 grains	14 grains	15 grains

[a] According to the manufacturer's brochure, dated 1933, each tablet of allonal contains 1 grain of alurate and 1⅔ grains of aminopyrine. The factor of aminopyrine in the toxicity cannot be evaluated in this report.

The thirteen patients were distributed as follows: Seven were hypersensitive to barbital, four to a dose of 5 grains (0.3 Gm.), two to a dose of 10 grains (0.65 Gm.) (one of them a chronic alcohol addict) and 15 grains in one (a morphine addict). Phenobarbital accounted for two patients, one who took 1½ grains (0.1 Gm.) daily for six days and one who was questionably sensitive, reported as taking 3 grains (0.2 Gm.). There were two cases of hypersusceptibility with amytal, one of 3 grains (0.2 Gm.) and one of 4½ grains (0.3 Gm.) and two cases with pentobarbital, 1½ and 3 grains (0.1 and 0.2 Gm.) respectively.

ADDICTION TO BARBITURATES

The thirteen hospitals together listed eighty-five cases under the heading of addiction to barbiturates, an incidence of about one case for every 15,000 admissions. No case of addiction was reported by three of the hospitals.

The relationship between addiction to barbiturates and addiction to all drugs (excluding alcohol) can be gained from data on the total number of patients with drug habit reported by six of the hospitals: Baylor University, Boston City, Peter Bent Brigham, New York Presbyterian and Michael Reese. During the decade 1928-1937 these clinics had 398 cases of addiction to all drugs (excluding chronic alcoholism), forty-three of which, or 10.8 per cent, involved barbiturates, about one of every nine addiction cases.

All but nine of the eighty-five addicts gave a reason for their habitual use of the barbiturates, and eight gave two reasons. More than two thirds, or fifty-two, used barbiturates for sedation or to combat insomnia. The next most common reasons, with eight patients (11 per cent) each, were substitution for alcoholism and to

4. Pohlisch and Panse: Schlafmittel-Missbrauch, p. 18.

5. Curran, F. J.: The Symptoms and Treatment of Barbiturate Intoxication and Psychoses, Am. J. Psychiat. **95**: 73 (July) 1938. Willcox.[6]

6. Willcox, William: Symposium on Hypnotics Including Barbiturates: Uses and Dangers of Hypnotic Drugs Other Than Alkaloids, Proc. Roy. Soc. Med. **27**: 489 (Feb.) 1934.

obtain an exhilarating effect ("spree"). Six of the addicts (8 per cent) were psychopathic. Five were morphine addicts. Four patients used barbiturates because of nervousness. Only one patient was reported to be epileptic. Eleven per cent of the patients gave two reasons.

The duration of the barbiturate addiction was reported for fifty-four of the addicts. Three of these (5.4 per cent) had used the drugs for more than fifteen years and another three for from ten to fifteen years. Two (3.6 per cent) had been addicts for from five to nine years. The most frequent period of duration with seventeen patients (33 per cent) was from one to four years. Sixteen more cases (29 per cent) had existed for an unstated number of "years." Nine (16 per cent) of the habits were of between one and eleven months' duration and four (7 per cent) were less than of one month's duration.

TABLE 3.—*Comparison of Fatal and Nonfatal Dosages in German Hospitals (1925-1932) (Charted from Data by Pohlisch and Panse [2])*

	Fatal					Nonfatal	
Drug	No. of Cases	%	No. of Cases of Known Dosage	Minimal Dosage, Grains	Median Dosage, Grains	No. of Cases	Maximal Dosage, Grains
Barbital.....	22	10.8	11	68	150	181	150
Phenobarbital..	16	10.5	6	36	90	136	130
Allonal *.....	2	20.0	2	36 tablets	36 tablets	8	36 tablets
(Alurate).....	..	....	..	36 grains	36 grains	...	36 grains
(Aminopyrine)..	..	....	..	54 grains	54 grains	...	54 grains

* According to Pohlisch and Panse, each tablet of allonal contains 0.16 Gm. (2½ grains) of drug, of which 0.06 Gm. (1 grain) is alurate and 0.1 Gm. (1½ grains) is aminopyrine. This is very similar to the contents of allonal tablets sold in the United States (table 2) previous to the recent change in formula following the advent of the new Food, Drug and Cosmetic Act in 1938. The product on the United States market now contains the less dangerous acetophenetidin in place of aminopyrine. The manufacturers, Hoffmann-LaRoche, Inc., state that allonal now has the following composition: 22.7 per cent alurate (allyl-isopropyl barbituric acid "Roche") and 68.2 per cent acetophenetidin.

The present hospital data throw but little light on the mental make-up of the addicts except as the number includes alcohol and morphine addicts and some psychopathic personality types. That the constitutional heritage of the individual is an important factor in the development of barbiturate habit is, however, amply demonstrated in the literature. Curran [5] says: "Any substance . . . which through its central action tends to soften the emotional stresses and to render less tedious the everyday experiences of life may be a factor in the development of habituation. . . . There is much evidence to support the thesis that the administration of sedative and hypnotic drugs to the emotionally unstable is fraught with the possibility of inducing habituation." Sands [7] has suggested that there are two types of individuals prone to develop barbiturate intoxication: (1) the manic-depressive types, who are most apt to take large doses with suicidal intent, and (2) the psychopathic constitutional types, who develop symptoms of chronic intoxication from habitual use of the drugs. McCowan [8] in England has observed that barbiturate addiction is practically confined to psychopaths, many of whom are morphine addicts; but he feels that addiction to barbiturates is apparently no greater than to the other hypnotics. This liability of psychopaths, McCowan cautions, must be kept in mind in prescribing for them. Robinson [9] has compared barbiturate addiction to alcoholism. He considers that in all types of habitual usage of drugs there is a strong psychogenic factor which registers a certain personality pattern.

Curran [5] observed that alcoholism was a factor in nearly one half (48 per cent) of fifty patients admitted to Bellevue Psychiatric Hospital because of intoxication by barbiturates. The next most common cause was menopausal symptoms. Marital difficulties came third. Other causes were insomnia, loss of money or occupation, neurotic symptoms or physical complaints including peptic ulcers, diarrhea and other intestinal disorders.

Pohlisch and Panse [10] analyzed 179 cases of chronic barbiturate poisoning. They found that seventy-five of the patients (43 per cent) were also users of opiates, fifty-five were frank morphine addicts and the remaining twenty used small amounts of morphine irregularly without developing true morphinism. The authors' classification of the mental status of these chronic users of barbiturates is given modified in table 4. The data for the two sexes, being very similar, have been combined. It will be noted that more than 70 per cent of the patients were put in the psychopathic personality class.

CHRONIC POISONING

No specific data were obtained from the thirteen hospitals with regard to chronic intoxication. Their records, however, do demonstrate that acute poisoning from an overdose is not uncommon, because six of the fifty-eight addicts died in this fashion.

There is evidence in the literature that the prolonged use of the barbiturates may be harmful; but there are other reports which indicate the relative innocuousness of such use. The daily use of phenobarbital by the epileptic is an example of the latter. It is generally agreed that this drug only infrequently results in toxic side actions. In this connection, Sollmann [11] states: "The ordinary dosage may be continued indefinitely without cumulation, craving or toxic effects. There may be rather excessive torpor and sleepiness, sometimes inebriation and rarely skin rashes." The literature contains many reports of isolated cases of skin rash, but there are no extensive data on the frequency of side actions in the epileptic. With the use of larger doses to control more severe cases, mental deterioration is reported; but how much of this is due to the disease rather than to the drug is difficult to evaluate. Hoge [12] reported that a woman had used from three to four

TABLE 4.—*Mental Status in Barbiturate Poisoning Modified from Pohlisch and Panse* *

	Acute Poisoning		Chronic Poisoning	
Mental Status	Number	Per Cent	Number	Per Cent
"Normal".....	24	3.4		
Psychopathic personality.....	413	58.4	127	70.9
Epilepsy.....	42	5.9	6	3.4
Psychoses.....	35	5.0	4	2.2
Debility and internal ailments...	26	3.7	7	3.9
Organic nervous disease.....	15	2.1	15	8.4
Undetermined.....	152	21.5	20	11.2
Totals.....	707		179	

* Schlafmittel-Missbrauch, pp. 18, 151.

7. Sands, I. J.: Barbital (Veronal) Intoxication, J. A. M. A. **81:** 1519 (Nov. 3) 1923.
8. McCowan, P. K.: Symposium on Hypnotics Including Barbiturates, Uses and Dangers of Hypnotic Drugs, Other Than Alkaloids, Proc. Roy. Soc. Med. **27:** 502 (Feb.) 1934.
9. Robinson, G. W., Jr.: Addiction to Barbituric Acid Derivatives, J. Missouri M. A. **34:** 374 (Oct.) 1937.
10. Pohlisch and Panse: Schlafmittel-Missbrauch, p. 151.
11. Sollmann, Torald: A Manual of Pharmacology, ed. 5, Philadelphia, W. B. Saunders Company, p. 739.
12. Hoge, S. F.: A Case of Prolonged Use of Barbiturate, Am. Med. **40:** 235 (July) 1934, cited by Curran.[5]

tablets (from three eighths to 6 grains, or from 0.024 to 0.4 Gm.) of amytal daily for several years and then had only moderate tachycardia and slight anemia. Polatin [13] gave eighty psychotic patients barbital in daily doses up to 30 grains (2 Gm.) over a continuous period of from one to twenty months and observed only a few toxic symptoms. All were relieved within twenty-four hours after withdrawal of the drug.

Such prompt clearing of minor toxic barbiturate effects is also quite uniformly observed on discontinuing the administration of phenobarbital to epileptic patients. In the epileptic, however, the severe psychic changes may only partly improve. The factor of histologic damage to nervous tissue in man by barbiturates has not been determined. In cats and monkeys, however, Mott, Woodhouse and Pickworth[14] have observed degenerative changes in nerve cells in the cerebellum, midbrain and spinal cord following daily oral feedings of barbital and phenobarbital for periods up to several weeks. In their opinion some of the cells were "damaged beyond hope of recovery." They used daily doses of from 2½ to 5 grains (0.16 to 0.32 Gm.) for cats and from 5 to 10 grains (0.32 to 0.65 Gm.) for monkeys, which generally exceeds human therapeutic dosage. Despite this, cats recovering from prolonged narcosis after ten to fourteen days "showed no observable impairment of normal activity and intelligence."

In contrast to the usual paucity of serious symptoms on continued daily therapeutic use of the barbiturates, Stone [15] reported two cases with marked toxic effects: 1. A professional man aged 45 stopped drinking because of alcoholic neuritis and started a barbiturate habit in an attempt to allay the resulting restlessness and insomnia. He developed visual, auditory and somatic hallucinations and marked persecutory delusions. On withdrawal of all sedation, recovery occurred slowly over more than three months. 2. An intelligent woman aged 59 received such heavy sedation for insomnia that she was forced to bed. For several months she had taken 3½ grains (0.23 Gm.) of sodium alurate several times a day until, when seen by Stone, she was mentally incompetent, doubly incontinent, markedly underweight and had to be spoon fed. Her spinal fluid was normal. When all medication was suspended, over a period of two months she gradually regained her weight, strength, ability to walk and sphincter control. But more than a year later, although physically robust, she was mentally childish. Stone raised the question whether, because of the patient's age, her mental deterioration might not be attributed to organic changes in the brain caused by the prolonged use of the barbiturates.[14]

Undoubtedly many more cases of chronic barbiturate poisoning have occurred, but few of these have been published.[16] This may perhaps be due to the reluctance of physicians to record the occasional isolated cases which they observe.

INVOLVEMENT IN AUTOMOBILE AND CRIMINAL OFFENSES

Barbiturates have been charged with being concerned in the increasing incidence of automobile accidents and criminal assaults. This seems logical, considering the sedative action of the drugs, but no literature is available on the subject. Letters of inquiry were, therefore, addressed to four leading toxicologists, three of whom replied.[17] Each stated that as yet he had no information on this topic.

SUMMARY

1. During the decade 1928-1937, thirteen hospitals with combined admissions of more than 1,250,000 received 643 cases of acute barbiturate poisoning.

2. One out of every 1,900 admissions was due to acute barbiturate intoxication.

3. Barbiturates were responsible for one seventh of the acute poisonings due to all drugs except alcohol and carbon monoxide.

4. The fatality rate in the cases of acute barbiturate poisoning was 7.3 per cent.

5. As each new barbiturate has been introduced clinically and has become publicized there has been a noticeable trend toward its use in poisoning cases.

6. The lowest fatal dose for barbital reported by these hospitals was 30 grains (2 Gm.); the median dose in fatal cases was 90 grains (6 Gm.). For phenobarbital the minimum fatal dose reported was 25 grains (1.7 Gm.); the median dose 142 grains (9.5 Gm.). The wider margin of toxicity for phenobarbital is probably accidental.

7. Hypersusceptibility to therapeutic doses of a barbiturate was charged in thirteen cases admitted to ten of the hospitals, about one case for every 90,000 admissions.

8. Addiction to barbiturates was the reason for admitting eighty-five patients out of the total of 1¼ millions admitted for all causes, about one barbiturate addict in every 15,000 admissions.

9. Barbiturates accounted for more than 10 per cent of all addiction cases, excluding chronic alcoholism, admitted to the thirteen hospitals.

10. Two thirds of the barbiturate addicts who gave information claimed that they became familiar with the drug through a physician.

11. Nearly a third of the addicts for whom the information was recorded developed craving when the barbiturate was withheld.

12. None showed any serious withdrawal symptoms.

13. No factual data could be obtained concerning the involvement of barbiturates in automobile accidents and criminal assaults, although from the nature of the actions of these drugs this might be expected.

This present study and that previously published [1] were undertaken to compile and analyze the available information on the evils of the promiscuous use of the barbiturates as suggested in a report to the House of Delegates of the American Medical Association in June 1937. The evidence clearly indicates that these drugs are responsible for many suicides, successful and attempted, as well as for many so-called "accidental" intoxications. As each new barbituric acid derivative becomes publicized, it soon becomes involved in cases of poisoning. Barbiturate addiction is fairly common. It makes up about one tenth of all drug addiction cases (excluding chronic alcoholism) received by hospitals in the larger cities. Despite the probable involvement of barbiturates in automobile accidents and criminal assaults, no data concerning such crimes are available.

13. Polatin, Phillip: Prolonged Sedation with Sodium Barbital, Psychiatric Quart. **11:** 213 (April) 1937, cited by Curran.[8]

14. Mott, F. W.; Woodhouse, D. L., and Pickworth, F. A.: Pathological Effects of Hypnotic Drugs upon the Central Nervous System of Animals, Brit. J. Exper. Path. **7:** 325 (Oct.) 1926.

15. Sone, C. W.: Some Undesirable Effects from Prolonged Use of Various Barbiturates, Ohio State M. J. **32:** 209 (March) 1936.

16. Purves-Stewart, James: Symposium on Hypnotics Including Barbiturates: Uses and Dangers of Hypnotic Drugs Other Than Alkaloids, Proc. Roy. Soc. Med. **27:** 503 (Feb.) 1934. Willcox.[9]

17. Personal communications to the author: A. O. Gettler, May 6, 1938; T. A. Gonzales, May 5, 1939; C. W. Muhlberger, May 10, 1938.

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SATURDAY, MAY 18, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

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BARBITAL AND ITS DERIVATIVES

Ever since urea was prepared synthetically by Wöhler in 1828 its derivatives have occupied an important place in medicine and in research. Urea, as an amino compound, may be readily combined with acids. A classic example of synthesizing is the so-called malonic acid synthesis, in which urea and malonic acid combine to form malonylurea (barbituric acid). This has been the basis of many of the hypnotic agents, particularly those belonging to the barbital series. By replacing the ethyl groups with other alkyl or aromatic groups it is possible theoretically to obtain more than 1,200 barbital derivatives.

In 1903 barbital (diethylbarbituric acid) was first introduced into medicine by Fischer and von Mering under the proprietary name of veronal. Its introduction was followed in 1913 by phenobarbital (luminal), which in turn was rapidly followed by other salts of the malonylureas. After the war of 1914-1918 a rush to produce modifications of the original compound that were not covered by German patents became widely apparent. Not until 1923, however, was the intravenous and intramuscular use of the soluble salts of barbital derivatives introduced. Since then the use of the malonylureas has been extensive among the medical profession and self administration by the public has brought about abuse. The effectiveness of barbital and certain of its derivatives is well recognized. Adverse results from their use, whether due to improper application or to so-called unavoidable accidents, have led to condemnation.

In a report previously published in THE JOURNAL[1] it was shown that "the evils of these drugs [the barbiturates] include habit formations, toxic cumulative action, their substitution for alcoholic beverages for drunken episodes, their use for successful as well as unsuccessful suicidal attempts, their improper use being a recognized causative factor in many motor accidents and their improper use being a recognized etiologic factor in some criminal assaults. . . ." In the same report it was further shown that for 1936 in the United States alone 231,167 pounds of barbiturates were manufactured, of which 174,188 pounds were sold (1 pound = 7,000 grains). The total number of suicidal deaths by the barbiturates (in 1936) was near to 300, about 4.2 per cent of all deaths caused by poisons and 0.66 per cent of all[1] suicidal methods. The trend has been upward especially since 1933.

The barbituric addiction is particularly vicious. Members of the medical profession will certainly not believe that barbiturates are free from possibility of addiction. Other undesirable results of barbiturate medication which are important, but commonly overlooked, are the toxic manifestations from (*a*) idiosyncrasy,[2] recognized since the introduction of barbital in 1903, and (*b*) long continued use, especially if the barbiturate is one of the longer acting members or if organic disease such as degeneration of the liver or vascular-renal system[3] is present.

Elsewhere in this issue of THE JOURNAL appear an article by Hambourger[4] presenting hospital data and a review[5] of the regulations of the sale of barbiturates. Restrictions enforced by law have become increasingly necessary with the education of the public to the possibilities that lie in the ingestion of the malonylurea derivatives. Attention was sharply drawn to this prob-

1. Hambourger, W. E.: A Study of the Promiscuous Use of the Barbiturates: Their Use in Suicides, J. A. M. A. **112**: 1340 (April 8) 1939.

2. Lundy, J. S., and Osterberg, A. E.: Review of the Literature on the Derivatives of Barbituric Acid, Proc. Staff Meet., Mayo Clin. (supp.) **4**: 386 (Dec. 18) 1929.

3. Scarlett, E. P., and MacNab, D. S.: Poisoning from Phenobarbital (Luminal), Canad. M. A. J. **33**: 635 (Dec.) 1935.

4. Hambourger, W. E.: The Promiscuous Use of the Barbiturates: II. Analysis of Hospital Data, this issue, page 2015.

5. Report of Bureau of Legal Medicine and Legislation, American Medical Association: Regulation of the Sale of Barbiturates by Statute, this issue, page 2029.

lem in 1933 by Willcox,[6] who discussed the existing dangers of barbiturates before the Royal Society of Medicine.

The Council on Pharmacy and Chemistry has long[7] adopted the attitude that the practice of using nonvolatile substances as anesthetics, especially in inexperienced hands, is not safe. Except for those agents which are rapidly eliminated such as pentothal sodium and evipal soluble, the Council still maintains this attitude. More rigid enforcement of restrictions on the prescribing of these potentially dangerous drugs has the whole-hearted approval of the Council and of THE JOURNAL.[8]

ERADICATING PINWORM INFESTATION

Effective therapy in the control of oxyuriasis is not yet available, though many therapeutic measures have been proposed. The fact that pinworm infestation is usually a familial condition involving several or all members of a family does not make it any easier to control. A recent contribution by the United States Public Health Service[1] presents the results of tests with santonin and hexylresorcinol. Santonin has been long recommended; hexylresorcinol was first used in 1932.[2] The tests were made on sixty-two persons, outpatients of a clinic for parasitic diseases maintained in one of the hospitals of Washington, D. C., consisting predominantly of children (75 per cent) of the lower economic level. Diagnosis in all cases was made by means of a special cellophane swab.[3] Inability to supervise posttreatment swab examinations closely did not permit making as many as seven such examinations in each case—the number which, according to other investigators, would detect 99 per cent of the total infestations.

Santonin was administered daily for ten days to twenty patients in doses varying, according to age and physical condition, from one-fourth to 1 grain (0.016 to 0.065 Gm.) and was found "relatively ineffective and unsatisfactory for the treatment of familial pinworm infestation," though eleven of the patients showed a negative reaction. However, three of these had had fewer than seven swab tests. Hexylresorcinol was tested in four different ways: by enemas, by peroral single doses, by a combination of peroral and enema treatment and in jelly form.

The report regards the administration of hexylresorcinol by enema as the treatment of choice. Single oral doses and the combined therapy, though tried out on fewer than five patients in each instance, were deemed "not dependably effective" or "not sufficiently encouraging." Hexylresorcinol jelly was found to be ineffective in preventing the migration of gravid females or in destroying gravid females or the viability of their ova. Hexylresorcinol was administered by enemas to twenty-seven patients in a 1:2,000 solution. Patients were given the drug in a suitable number of vials and instructed to follow up a preliminary soapsuds enema with the hexylresorcinol treatment (one quart for adults; as much as could be retained for children). Of the twenty-seven patients, eighteen showed a negative reaction, four of these "doubtfully" so. Yet the report says: "Considering the multiple factors involved in attempting an appraisal of the experimental results, we are of the opinion that the data show hexylresorcinol enemas to be of definite value if used in repeated treatments over a sufficient period of time. For satisfactory results in most cases, it would appear that the use of at least ten enemas spaced over a period of three weeks is necessary." Two of the patients, however, who received twelve enemas were still positive following the treatment. The report also says: "Better results might have been secured had we administered hexylresorcinol orally one or more times during the period of treatment with enemas. However, this was not done because of our inability to supervise the treatments closely." The drawbacks of hexylresorcinol treatments, it is pointed out, consist in the expensiveness of the drug and the necessity of applying treatments over considerable time. The report states that most of the anal ointments recommended in medical literature are of little or no aid in the control of pinworm infestation, though some of them appear to be of value in allaying pruritus. Nonmedicated enemas, including soapsuds and saline enemas, are regarded as occasionally of advantage for infants and young children too small to take oral therapy satisfactorily, if repeated every other night for at least three to four weeks, in some cases longer.

PRIMITIVE TUBERCULOSIS

The distinctive aspects presented by tuberculosis in primitive races have often been the subject of investigation and discussion. Recently Cummins,[1] who is director of research of the Welsh National Memorial Association and experienced in the clinical features of tuberculosis among African Negroes, has pointed out again that the individual or race without previous contact with tuberculosis lacks resisting power. The power to resist is gained quickly, however, among civilized people, he says, because their ancestors have been subjected to a process of natural selection and only those have survived whose resistance is high as measured by their rapid

6. Willcox, Sir W. H.: Discussion on the Uses and Dangers of Hypnotic Drugs Other Than Alkaloids, Proc. Roy. Soc. Med. **27**: 489 (Feb.) 1934.

7. Nonvolatile Substances as Anesthetics, Current Comment, J. A. M. A. **95**: 1430 (Nov.) 1930.

8. Reprints of the reports of the Council on Pharmacy and Chemistry and of the Bureau of Legal Medicine and Legislation will be available at 15 cents each. In order to estimate the number of copies necessary, it is asked that requests be sent in immediately.

1. Wright, W. H.; Brady, F. J., and Bozicevich, John: Studies on Oxyuriasis, Pub. Health Rep. **54**: 2005 (Nov. 10) 1939.

2. Brown, H. W.: Treatment of Pinworm (Enterobius Vermicularis) Infestation with Hexylresorcinol, Proc. Soc. Exper. Biol. & Med. **30**: 221 (Nov.) 1932.

3. Hall, M. C.: Studies on Oxyuriasis, Am. J. Trop. Med. **17**: 445 (May) 1937.

1. Cummins, S. L.: Primitive Tuberculosis, London, John Bale Medical Publications, 1939.

elaboration of antibodies. The "primitive man" according to Cummins has not had the advantage of such selection and is therefore at a much lower point of the scale in ability to elaborate resistance. Nevertheless the biologic reaction to hypersensitivity is present and is rapidly produced following the entrance of the tubercle bacillus. Under favorable circumstances of nutrition and leisure the chances of survival are good even among primitive peoples unless subjected to overwhelming access of germs.

Cummins divides immunologic stages of tuberculosis as follows: 1. Indifference: no appreciable hypersensitivity or immunity. 2. Intolerance: (*a*) potential intolerance, (*b*) active intolerance. 3. Tolerance: (*a*) negative tolerance, (*b*) positive tolerance. This is further explained as follows: "The first phase of indifference was to be observed only at the beginning of a primary infection. The second intolerance might reveal itself either as a result of testing persons of European stock with tuberculin, when it would appear in the form of intolerance to that substance, though all the time the person was immune to the ordinary degree of infection, autogenous or exogenous, which usually reaches the body of one exposed to town life, or as 'active intolerance,' the activity revealing itself as a very high reaction to tuberculin and a tendency to violent reaction to the bacillus already in the body but stirred up to freedom in the tissues through unaccustomed hard work or the effects of new surroundings. Tolerance was a term for failure (or almost failure) to react to tuberculin and it was thought to be of two kinds: 'negative,' where hypersensitivity and immunity had been swamped by infection (anergy), a form well known in the last stages of tuberculous disease, and 'positive,' where hypersensitivity had been lost but immunity was operative (adiaphory), a form which is seldom observed but which can be brought about by desensitization with tuberculin or by autotuberculin in some instances. The weakness of these definitions is that they deal chiefly with extreme cases and leave out the essentially important intermediate stages. The term 'potential intolerance,' however, has much importance, as it admits that the ordinary person, reacting to tuberculin when tested but quite free from the disease tuberculosis, may, under certain circumstances, break down into the disease though he is now so healthy."

In his final conclusions, Cummins writes: "Tuberculosis will always be the enemy of primitive races and will take its toll the more heavily the more rapid is their emergence from primitive to civilized conditions." This seems to be a generalization not yet proved by facts and figures. There is for instance the Japanese population, certainly living for a long time on its own soil and surely not a "virgin population" to tuberculosis but still paying a high toll in mortality, more than double that of the United States, white and colored population together. The course of epidemiology in tuberculosis cannot be explained so easily. Cummins furthermore does not take into account the steadily varying influence of social environment and social biologic factors which may diminish or increase the normal resistance of a population group and thus probably play a decisive part in epidemiology.

Although the constitutional influence on tuberculosis in primitive races may be important, complex questions of social environment are involved as well, and the hazard of too much speculation should be avoided.

Current Comment

A COMMENDABLE PROJECT FOR GRADUATE EDUCATION IN TUBERCULOSIS

Frequently THE JOURNAL has pointed out the manner in which physicians themselves do their utmost to keep abreast of newer methods in the diagnosis and treatment of disease. A project recently developed by the National Medical Association—national organization of Negro physicians and medical workers—for dissemination of further information regarding tuberculosis and for the control of this condition among Negroes in Chicago deserves special attention. By arrangement with the officials of the Municipal Tuberculosis Sanitarium a postgraduate school was set up in the South Side Municipal Tuberculosis Sanitarium and Dispensary in which, for four days a week and for two hours daily, members of the staff of the Municipal Tuberculosis Sanitarium gave instruction to Negro physicians. More than 90 per cent of the physicians who had registered for the course attended each of these sessions. The success of the project has been so great that it is now planned to continue similar courses for three months, four times a year. Opportunities are thus given to twenty physicians during each period for special training in tuberculosis. Moreover, arrangements have been made for an x-ray survey of those districts in Chicago in which the mortality and morbidity are highest. The Municipal Tuberculosis Sanitarium has a mobile x-ray truck equipped with a lens so that six centimeter films can be taken. Furthermore, leading members of the National Medical Association are devoting large amounts of their time for addresses to church groups, insurance groups, and civic and social groups, urging cooperation in this effort. Finally, through the cooperation of a "home for the friendless" organization, a building formerly occupied by that organization has been deeded to the Municipal Tuberculosis Sanitarium to provide facilities for 400 Negro patients. A large mass meeting for the promotion of these projects and for the raising of additional funds will be held in the near future. Movements of this type are a model of that spirit in the American democracy which causes the citizens to seek to help themselves and to accomplish the utmost that can be accomplished by individual effort before throwing the burden on governmental agencies.

ORGANIZATION SECTION

NATIONAL CONFERENCE ON MEDICAL NOMENCLATURE

Held in Chicago, March 1, 1940

DR. HAVEN EMERSON, New York, in the Chair

Purpose of the Conference

CHAIRMAN EMERSON: The undertaking we have to develop today began, I believe, in April 1929 in Berlin, when a half dozen physicians and statisticians met at the call of the League of Nations. The object of their meeting was to determine how international statistics could be more effectively used. On that program was the question of developing within nations a standard nomenclature and later a common international one. The meeting agreed, with the approval of the League of Nations' Health Section, to ask each nation to prepare within the next ten years its own idea of a desirable listing of all diseases by etiology and anatomic site for purposes of permanent classification. What we are now engaged on is the first decennial revision of the effort made by the voluntary group, which was supported by financial aid from various funds, insurance companies and others, some years ago.

Trends in Medical Terminology

DR. MORRIS FISHBEIN, Chicago: The taking over of the editing and publishing of the Standard Nomenclature by the American Medical Association was another of the tasks which have been taken up from time to time when others found it impossible to carry them on. All are familiar with the publication of the *Quarterly Cumulative Index Medicus,* which was taken over by the American Medical Association after the government, the Carnegie Foundation and other groups found it impossible to continue to carry it on. It has been continued by the Association for many years at an annual loss of about $40,000.

The publication of a Standard Nomenclature is work of a similar type, necessary for the advancement of medical science through the development of a common language and a system whereby cases of disease may be suitably recorded. As I have traveled about the country and talked with professors of medicine and surgery, librarians and others, the main request I hear seems to be toward the greatest possible simplification of a standard terminology, toward the elimination, if possible, of as many unnecessary terms as can be accomplished. Again, there is definitely a movement in scientific nomenclature throughout the world toward eliminating eponyms. In general, the use of the eponym is not scientific. It is like the trade name on a "patent medicine" or a food. Eponyms are not truly descriptive, and it has seemed to me that scientific language should be descriptive as far as possible. To that extent I believe we ought to consider eliminating eponyms from any Standard Nomenclature.

There is a tendency nowadays to eliminate, as far as possible, terms from foreign languages in an effort to get a standard English nomenclature for use in institutions in the United States, Canada and Great Britain. Finally, in order to make this useful to readers whose minds run along historical or classical lines it might be desirable to include in the book, if not a glossary, a table of eponyms and foreign terms which have been translated into English terms, with a cross reference to the place at which the standard or adopted term is listed.

CHAIRMAN EMERSON: Great advance has been made in both the International List of Causes of Death and the present Nomenclature in elimination of names that are not precisely descriptive. We have had to make some concessions to affection, to history, to sentiment and to international usage, but so far as possible that practice has been followed.

Purposes, Function and Use of Standard Classified Nomenclature of Disease

DR. GEORGE BAEHR, New York: The Standard Classified Nomenclature of Disease is now employed in almost all important hospitals and medical schools of the United States and Canada. The success of this American enterprise is largely due to the manner in which it was prepared during the years preceding the publication of the first edition (1928-1933). It was initiated and carried to completion by the collaboration of all important national societies representing medicine, surgery and the specialties. Previously there had been hundreds of local efforts. As they multiplied in number and variety, their many authors failed to appreciate that they were modifications of preexisting efforts which merely perpetrated illogical and overlapping methods of classification, that each was colored by peculiarly local hospital needs and that in their separate parts they did not express the ideas or meet the demands of advanced experts in the highly specialized branches of medicine and surgery.

The purpose of a nomenclature is to encourage the use of expressive terms, the meaning of which can be accepted universally without ambiguity. The best term is the one which most completely expresses the nature of the disease. The primary purpose of a classified nomenclature is to arrange the diseases in a logical and orderly manner so that there may be no possibility of overlapping one another. Now that almost all important hospitals use the Standard Classified Nomenclature, the disease files of their record rooms are mutually interchangeable. Their clinical experiences are readily available for study as well as for comparison with the experiences of other institutions. The chief virtue of the Standard Classified Nomenclature of Disease is that from beginning to end it never departs from the simple construction of its basic schema. Every disease is described and classified topographically, in terms of the tissue or organ where it is principally manifested, and also into etiologic categories. This has permitted the use of a simple library decimal system which facilitates record room filing.

There has been some complaint that the six or more numbers necessary to designate a disease or injury do not lend themselves as readily for punch card recording as some simpler numerical system. It must be remembered that the primary purpose of the Standard Nomenclature is for clinical use. It is to encourage uniformity and accuracy in clinical expression. Our dual decimal system for the numerical designation of the diseases permits the employment of the Standard Classified Nomenclature of Disease as a clinical discipline, not only for fourth year medical students who as clinical clerks are being taught to think and to express themselves accurately, but also often as a much needed clinical discipline for the attending staff of the hospital. The resistance of clinicians to making the little extra effort required by the use of the Standard Nomenclature is soon replaced by appreciation of an orderly disease file in the hospital record room. In 1937, on behalf of the National Conference, I proposed to turn over to the American Medical Association the permanent responsibility for the Nomenclature. In effecting the transfer the hope was expressed that the Association would continue to work through the medium of a national conference, composed of all the national clinical societies, the federal medical services and other interested organizations. Suggestions have been advanced that the Standard Classified Nomenclature of Disease is too large. A significant abbreviation of the book can be accomplished only by omitting thousands of diseases of rarer occurrence. The volume would then lose its value even for small

hospitals. The size of the volume and the number of terms it contains do not complicate the problems of the record room clerk or of the hospital physicians. The size and complexity of the disease file of a record room are not determined by the size of the Standard Nomenclature. There are some who think the Standard Nomenclature is not large enough and who demand an opportunity to record various clinical manifestations of disease or even laboratory observations. This is beyond the scope of a nomenclature of disease. A criticism of the Nomenclature is that it does not lend itself readily to cross reference to the rubrics of the International List of the Causes of Death. After each disease, the appropriate code number of the international list is to be found. This can be transferred to punch cards for statistical tabulation. In this manner morbidity can be compared statistically with information regarding mortality.

Although this third edition of the Standard Classified Nomenclature of Disease may not require revision for ten years, a central staff must continue to be maintained as the clearing house for the exchange of opinions on the use and the significance of both new and old diagnostic terms.

International Nomenclature and the International List of Causes of Death

DR. HALBERT L. DUNN, Washington, D. C., chief of the Division of Vital Statistics of the Bureau of the Census: The revision in Paris in the fall of 1938 was the result, as far as the League of Nations goes, of several years of intensive work by a committee of the American Public Health Association, a subcommittee of the Committee on Standards called the Subcommittee on Certified Accuracy of Causes of Death. Dr. Emerson was chairman of that committee and Dr. Baehr was a member of it. The new list varies much from the old, particularly in the rubrics involved with heart disease and probably with accidents, and rheumatic involvement of the heart. The detailed list is included in the Physicians' Handbook, which has just been published with an index. For all relatively simple purposes the handbook itself can be used as a coding mechanism for the list. The book has gone to press and should be available within a month or a month and a half for those who want it. We have a sufficient quantity of the Physicians' Handbook to distribute to the physicians of the country and have enough over to give medical students and to use for training purposes in years to come.

The publication of the International List in book form, which will contain in it the complete joint cause manual and the special rules for coding joint causes, will be available only at purchase, except for about four or five thousand copies which will be placed in laboratories and hospital record rooms where coding is a daily function. The International List is not a nomenclature like the one which we have met to consider. This list is used to produce statistics around certain definite, fixed categories rather than a classification built to establish the cause of disease or to locate the specific case that a particular physician might be interested in reviewing. Because it has that purpose, it is necessary to establish an index to the International List. The deaths which are recorded in this list come from many sources. Many of the death certificates are filled out with unsatisfactory terminology. We try to get it in better shape, but when one can't get a better term that particular cause of death, unsatisfactory though it is, must be placed somewhere in this list. It must be placed in a consistent category; otherwise one wouldn't know what the rubrics contained. If it is too unsatisfactory, it is simply placed in a miscellaneous category, which means we don't know much about the content of meaning of that particular rubric.

Another problem is what to do with multiple causes of death when they are returned on the death certificate. The way that has been done, as far as our own country goes, is to form an arbitrary system of selection which has been called a Manual of Joint Causes of Death. Some of the International List rubrics will show great consistency in the usage of medical terms. Out of the typhoid rubric, 99 per cent of those terms will come in as typhoid fever. There are other rubrics in which there will be gross discrepancy with reference to how doctors use the original descriptive term. The homogeneity of the various rubrics is going to be studied intensively as a part of the future development of this list. That material will be in the hands of the next committee on certified causes as it starts to work, so that it can have available a picture of the consistency of medical usage of these terms.

There is constant pressure for additions to the International List. The pressure results primarily from two conflicting points of view. One is the necessity, in statistical studies of death, to keep comparability with the past. It is necessary, even as we change the list, to keep up with medical practice, new medical terminology. We don't like to make it impossible, in a revision of this list, to find out the statistics in the same way as they had been reported in the past. It breaks the continuity of studies to do this. However, the pressure for change, in order to get the material into a new form which will be more useful in the advancement of the science of medicine, must be taken into consideration. This has resulted in many breakdowns of those rubrics, which must be considered as time goes on in relation to comparability with the past and the values inherent in the new medical point of view. Simplification of the list will depend on such considerations. We have to make adjustments, and when their significance becomes realized we must break with the past and put up appropriate bridges which will help us interpret the statistics of the future with the past. That perhaps covers the main considerations of where the list fits into this nomenclature.

The standard Nomenclature is adapted to the needs of physicians in their hospital practice. It is not adapted for a statistical tabulation of the type that the International List has been adjusted to care for. The physician is not primarily interested in such use at this time, but there are many groups that are interested especially in the hospital insurance field. They need it desperately. It ramifies through all the evaluation of the risks involved in hospitalization of certain diseases. When such a list is created, it becomes essential that that list be correlated with the International List of Causes of Death. Without such a correlation it will be impossible to get case fatality rates which are desirabie. There are many errors—at least we think they are errors—in the way the International List numbers have been placed on the terms in this book. I should like to offer all the help we can give to making that kind of correction when the new volume is edited.

DISCUSSION ON PAPERS OF DRS. FISHBEIN, BAEHR AND DUNN

DR. HOWARD FOX, New York (American Dermatological Association): Dr. Baehr said that the Nomenclature is used in a great many of our best hospitals. It has been accepted also by most of the colleges and important national organizations. In editing my periodical I insist that every name follow the Standard Classified Nomenclature of Disease. Textbook writers are bound by the same rules, but I have found that a good many of them coin new names of their own. I would make a plea for every one to follow, as far as possible, this book. In looking over my own special chapter, I have been astounded to see the diseases that are given as causes of death included in the International List. In this list are such diseases as acne milium (prickly heat), webbed fingers and keratosis pilaris, which merely means rough skin. The Chairman told me before we came in that those are included because some one made that diagnosis as the cause of death, and they must be there. Just because some one gave a ridiculous cause of death, we should not continue to include this nonsense in the next revision of the book.

MISS DOROTHY L. KURTZ, New York: Our staff at the Columbia Presbyterian Medical Center wished me to urge this conference to consider some practical answer to the criticism that the Nomenclature is too complicated. Every time I talk to members of the staff I hear that when they have to make a secondary diagnosis outside their own field they feel at a loss. They don't feel that they should spend the time to select the right term, and they often omit it or merely guess at it. That admission is made repeatedly by the best men on the staff. Medical record librarians from different parts of the country express the opinion that their staffs go through the

same experience. A group of men from the Public Health Service and the Immigration Service visited our hospital to see if they might adopt the nomenclature for their purposes, but although they admired its scholarly quality it was utterly unsuited to their purposes. One of the advantages of the Nomenclature is that it comprises the preferences of various specialties. But to ask a general physician to be familiar with a specialty, or to ask one specialist to be familiar with another specialty to the extent that the original one was, is not working. Possibly an abridged form that would suit the public health groups might offer a solution. If that should be decided on, it might be possible in the hospitals to have a complete book in the record department for reference and to have each of the services furnished with the abridged list, each one with its own special chapters from the original book. That would also answer the complaint that it is too bulky. Possibly a committee could study it and offer a more carefully thought out solution. If hospitals that are well regulated and familiar with the book find that it is quite common to omit terms because they can't bother to find them in other than their own fields, this represents another point in which the Nomenclature is not meeting its aims. I feel that is as important as a revision and further refinement of the book in its present form.

DR. MONTAGUE L. BOYD, Atlanta, Ga. (American Urological Association): I have been working with the Nomenclature from the beginning. In fact, when the National Conference took over the Nomenclature I began adapting the nomenclature I had already devised for the American Urological Association to the etiologic and regional classification prepared by Drs. Emerson and Baehr. My problem has been from the clinician's side, to get the urologists interested in the Nomenclature, which is almost an impossibility as it is at present. The American Urological Association has published a nomenclature for the urologist in which terms are listed under the organs in alphabetical order, with an elaboration and references to the proper term to be used, when a man looks up something like a Hunner ulcer. I am interested in whether these terms are to be limited or whether you are going to add to them. From an educational standpoint the essential thing is for the specialist to add to the terms and have available all of the diseases to which he can refer under his specialty. Since the last publication of the Nomenclature, I have suggested sixty additional terms to the Standard Classified Nomenclature and I have forty-five more here to add. I think this conference ought to take some stand on that matter.

CHAIRMAN EMERSON: Three matters have been brought up for critical opinion. One of them is whether there should be an abridged list and, if so, how it should be made. Another one is how we can simplify the relationship to the International List of Causes of Death. And the third is whether there shall be a mechanism by which an all inclusive encyclopedia for the specialist shall be included with the International List or the Standard Nomenclature. These are problems which will have to be referred to special committees.

DR. GEORGE BAEHR, New York: In speaking of abridgment do you mean the preparation of a tabular list for statistical recording or an abridged Classified Nomenclature of Disease?

CHAIRMAN EMERSON: I gather that the demand has been that there should be for current use in hospitals not only the complete Standard Classified Nomenclature but an abridged list for usual ward use, which could be expanded as desired.

DR. MORRIS FISHBEIN, Chicago: We should keep in mind the possibilities in the development of a book like the Standard Nomenclature and also the practicabilities in the situation and the special needs. I would like to emphasize the point made by Dr. Dunn. Language is not static and knowledge in medicine is not static, and it becomes necessary to carry over from the past into the present, and to contemplate, at the same time, the future. Such lists are constantly in a state of evolution. We do not set up a Standard Nomenclature today that we know is going to be good five years from now. We take it for granted that it is necessary constantly to keep on advancing, but we know also that no group can advance much faster than the majority in the group. The purpose of this Standard Nomenclature, as I see it, is to carry the profession forward to some extent, and merely because a considerable number of clinicians working in the wards do not care to take the time to write scientific diagnoses, as listed in the Standard Nomenclature, but prefer to use some term which they have carried with them from their student days is no reason why we should not attempt to make progress by encouraging people to step along with the advancement of the profession. We make advancement only by setting standards high and then by endeavoring to encourage the profession to follow those standards. That is the purpose of the Standard Nomenclature. There is constantly, at the same time, an effort to drag back; constantly a group which says "You are going ahead too fast; you shouldn't have raised the standard of medical education as far as you have. What we really need are one year nurses and two year doctors." We have all of these motives working at present in relationship to the development of the Nomenclature. It is going to be impossible, from a printing point of view and from meeting costs, to endeavor to prepare several different books: one book of a few terms that will be used by clinicians, another book of considerable scope that would be used in the hospital library and in the office of the record librarian, a third book which would attempt to fit the Standard Nomenclature to the International List of Causes of Death. We have to get out one book which will represent a reasonable standard. We must take advantage of Dr. Dunn's offer to fit that, as nearly as possible, with the International List of Causes of Death. Then we must encourage our record librarians to do their utmost with the clinicians to make them use this standard book.

DR. HALBERT L. DUNN, Washington, D. C. (American Statistical Association): This matter of accepted terminology has a basic, philosophic issue underlying it. That is not a committee problem. We have tried, in a way, to make a sort of nomenclature out of the Cause of Death List by saying that we will limit the list to certain approved terms which we like. We have put those right into our nomenclature but, at the same time, we recognize that we are going to get a lot of others which, while not approved terms, are going to be coded in such and such a way. So they stick indefinitely. When a term isn't approved that doesn't necessarily mean it is an unsatisfactory term. It might be a poor term and be loosely used. Again, it might be the term that is coming into vogue and that will be used by everybody five years from now. What makes that term satisfactory depends on how many people use it and whether they use it the same way, and not whether we like it from the English point of view. That is the way the dictionary changes, and that is what we face. The whole question is whether we can create something that is rigid in terminology and make doctors fit their diagnoses into it, when frequently they might not want to put them there. This deserves the deep consideration of this conference, because the success of the Nomenclature depends on it. I think we have a philosophical question that has to be solved by the whole group.

DR. BAEHR: On the part of clinicians there is a great impatience with the inadequacies in the International List of Causes of Death and with the fact that terms are found scattered under different rubrics that really belong together. This is because when one tries to get international agreement between forward looking and backward looking countries it is often difficult to achieve a compromise which means moving forward. In the conference in Paris in 1938 much was achieved, so that now disease conditions which, though still scattered, come traditionally under different rubrics can be brought together by the vital statistician, so that one can know the incidence of rheumatic fever as expressed in mortality reports. The movement to secure international usage of a nomenclature for morbidity had its origin some years ago in the International Hospital Association, which, recognizing the need for uniform usage in hospital record rooms, appointed a committee on which various countries had representatives. Sir Humphry Rolleston was designated by the British Ministry of Health; Dr. Achard, who has long been interested in this subject and is secretary of the French Academy of Medi-

cine; and Bastianelli was designated by the Italian government. There were about eight or ten governments that delegated representatives to work on this problem. The basic schema of our Standard Nomenclature was universally acknowledged as the satisfactory basis on which to build an International Nomenclature. No matter what the diseases might be called in different countries, officially the pigeonhole was there, so that morbidity information between countries ultimately could be exchanged with a certain degree of comparability. The International List of Causes of Death was primarily devised by vital statisticians, with relatively little organized assistance on the part of clinicians. Under the influence of Drs. Dunn and Emerson a beginning was made toward putting some clinical interest into the International List and obtaining the advice of clinicians. More of the clinical background in the past would have served to improve the applicable usefulness of the International List of Causes of Death.

CHAIRMAN EMERSON: I should say it would take at least thirty years—that is, three international conferences—before anything in the way of an international agreement on nomenclature of disease could be accomplished. We have been working since 1890 on the International List, and each ten years marks a distinct advance in usefulness. We are at the same point now with regard to nomenclature at which we were when the first International List was adopted at the meeting in Chicago in 1890. We must establish our philosophy at this time. I think we shall find that there are ways which will make it possible, within one publication, to serve the needs that have been suggested here.

A Standard Nomenclature of Operations

DR. H. PERRY JENKINS, Chicago: There have been several operative terminologies published in recent years, each organized in a somewhat different manner and presenting different terminologic points of view. The Surgical Nomenclature of the New York Hospital, devised by Dr. Ray and Miss Lincoln, employs a system of code numbering for different operations and is classified into a system comparable to the disease nomenclature. It more closely resembles the Standard Disease Nomenclature than other operative terminology.

In preparing a standard operative terminology, the most useful features of the several publications which have appeared thus far should be consolidated. It would be desirable to have it classified into systems, as well as organs, in the same manner in which the Standard Nomenclature of Disease is classified. Under each separate organ would come the classification of operations. The names of operations by the Western Surgical Society, edited by Dr. Black, combines the simple English term on one side of the page and the regular Latin term, or the name of the organ plus the suffix "ectomy" or "otomy" adjacent or parallel to the simple English term. That feature should be incorporated into any ultimate standard operative terminology. There is the matter of how to handle different operations. For example, there are operations that may be done in multiple stages. Should all those operations be filed separately? Then there is the question of terms that lack specificity. To be scientific is another thing that should be taken into consideration in connection with a standard operative terminology.

DISCUSSION

CHAIRMAN EMERSON: Dr. Jenkins, do you believe it is desirable to include in such a publication as this either a supplementary or an interpolative list which will make it possible to classify operations under some basis yet to be determined?

DR. H. PERRY JENKINS, Chicago: Either as a separate book or as a supplement, yes.

DR. EDWIN P. JORDAN, Chicago (American Medical Association): There has been a considerable demand for a surgical terminology. Most of that demand has taken the form of a request for something which could be related to the Standard Nomenclature of Disease. At present there are many surgical terminologies. The publishers of several surgical terminologies have indicated a desire to merge their interests in something which could be more generally accepted. Several people have indicated their willingness to cooperate in attempting to prepare such a volume or list or terminology which would try to combine the better points of them all. Dr. Jenkins has compiled one terminology of operations which is widely used, Dr. Ray another, and Dr. Ponton another. All of them have indicated that the larger interests of the question of terminology could be best served by attempting to adopt some standard terminology.

DR. WARREN P. MORRILL, Chicago (American Hospital Association): The philosophy of the Standard Nomenclature was to erect a nomenclature on a definitely scientific basis, without much effort to accommodate it to common usage. That has, so far, proved the most difficult hurdle in securing its use. If we are going to add an operative nomenclature—surgery is only one form of therapy—why not set up one for sulfanilamide, for instance, sulfapyridine, mercury, arsenic, quinine? There is no stopping place when we start to put therapy in with the nomenclature of disease.

DR. KELLOGG SPEED, Chicago: I speak on behalf of Names of Surgical Operations, devised by the Western Surgical Association, printed in 1935, the committee for the preparation of which I was a member. We would welcome an opportunity to have surgical nomenclature added to this standard book on Nomenclature of Disease. We found in our efforts that there were 3,300 or more names of operations given in Dorland's dictionary in 1933. It is difficult for the clinician to use so many intelligently, for the student to learn them or for the record librarian to adopt them in filing. We therefore made an attempt to reduce the number on a simple English basis to about 700 names, which may be amplified according to the character of the operation. We took the opportunity to eliminate all proper names from surgical procedures, thus bringing it down to a basis which might be used in international usage. We found great difficulty, from a philologic basis, in adapting the compound words with Greek and Latin roots to a common basis which was correct, and we finally had to adopt the idea that usage and custom is what makes the word, what makes the description and names the operation.

DR. BRONSON S. RAY, New York: I am one of the compilers of the New York Hospital Nomenclature of Operations that has been referred to. We felt a need for such an index and nomenclature in 1935 and set about finding whose we could adopt. Dissatisfied with any one else's, we built our own entirely by the method on which the Disease Nomenclature had been built. The Disease Nomenclature includes two groups of numbers, topographic and etiologic. The Operative Index and Nomenclature we devised has also two numbers, topographic and the procedure which corresponds to the etiologic division. With this method we could handle most of the difficulties that arose. We published a book in 1938 and sent complimentary copies to all the professors of surgery in the medical schools of the country and to the record librarians of about 250 associated hospitals. We have been using it and have indexed the operations in our hospital for four years. About 100 other hospitals have also used it for a year or longer. We have found no great difficulty in using it, nor have other hospitals. Some hospitals have complained that it has not been inclusive enough, others have complained that it is too inclusive, and still others want to make some arrangement whereby nonsurgical procedures can be included in it. Because other hospitals began to use this index, we began to feel a little uneasy about the situation, because if a number of hospitals set such an index up and within a short time a standard one for the country of a different sort was made, it would mean that all these hospitals would have to discard what they had already done. My purpose in saying anything is to urge the formation of a Standard Nomenclature of Operations. All hospitals in the country are anxious that such a standard be established.

DR. M. T. MACEACHERN, Chicago (American College of Surgeons): There is a tremendous demand for a good Nomenclature of Operations. I have six nomenclatures in my library. I would like to speak on behalf of Dr. Carl Lenhart, head of the department of surgery at the University Hospitals in Cleveland. They have developed a good one and I am sure they would like to cooperate in a joint plan of getting one out that would be of a standard nature. I think we should do it and use

the splendid material that has been prepared by the New York Hospital, by Dr. Jenkins, by Dr. Lenhart and by others.

DR. THOMAS R. PONTON, Chicago: I believe my Nomenclature of Operations was the first to be published. Of the many Nomenclatures of Operations that have been promulgated, in my opinion the best that has been made is an unpublished one, the semifinal revision of the Western Surgical Association Nomenclature. Unfortunately, when it came to the point of publication I believe the simplification was carried too far. The question of a condensed nomenclature has been discussed. I don't believe it is possible. I think we have to give the complete nomenclature as we believe it is correct. We object to having our nomenclature called "The Ponton." It is "The Alphabetical." We object to the use of personal names. I have been an advocate of the Latin in the nomenclature of disease, but I have always done it with my tongue in my cheek. The Standard Classified Nomenclature, the Alphabetical, the Massachusetts General, the Anatomical, or any of the nomenclatures, except the BNA, are none of them in Latin. Pure Latin, if we could use it, would be so pedantic that it would destroy our entire objective. On the other hand, there is no such thing as an English terminology of disease. I think a better way of describing it is to call it Latinized. I am wholly behind this movement. I believe that by the American Medical Association taking over the Standard Classified Nomenclature of Disease it will be possible to overcome the great difficulty in getting nomenclature adopted.

The Adaptation of the Standard Classified Nomenclature of Disease to Hospital Morbidity Reports

E. H. L. CORWIN, PH.D., New York (read in absentia): Hospital morbidity statistics apart from mortality statistics are of service to the hospitals and to the community. As to the modus operandi, the experience of the Peter Bent Brigham Hospital, the Mayo Clinic, the Johns Hopkins Hospital and others, is of much value. So also is the experience of three attempts in New York City at collective gathering of hospital data. The first demonstration of the kind was made in New York under the direction of the Hospital Information and Service Bureau of the United Hospital Fund in 1923 in cooperation with six hospitals. In this experiment the simple method suggested by Bolduan was followed. The participating hospitals agreed to send certain information concerning their discharged patients using a form of certificate agreed on and these certificates were edited by a medical registrar in the same way as death certificates are registered by a registrar of vital statistics. There was no uniformity in the manner in which diagnoses or other data were reported from the cooperating hospitals. The second study on a much larger scale was undertaken under a WPA grant by the Research Division of the Welfare Council of New York City. It covered the entire annual experience of 113 hospitals in 1933 and comprised data pertaining to approximately 576,000 patients. Here again there was no uniformity in the reported facts and, as in the former study, a method of procedure had to be worked out to make possible a practical approach to the problem of classification. One of the valuable results of this experiment is the "Classified List of Diagnosis for Hospital Morbidity Reporting" published by the Welfare Council of New York City. This is based roughly on the Standard Classified Nomenclature of Disease, although the arrangement of the group diagnoses followed the International List of Causes of Death as far as possible. The third experiment is that which has been carried on for the last ten years by the Division of Medical Records and Statistics of the Department of Hospitals since 1929, when all the municipal hospitals in the city were consolidated into one department. The work of that division under Dr. Caroline Martin is the most noteworthy contribution in the field of hospital morbidity statistics.

Only recently has the Standard Classified Nomenclature been introduced in all the municipal hospitals and this has, no doubt, simplified the task of the central statistical office. For broad statistical tabulations in contradistinction to the precise individual clinical entries, it may not be possible to follow the Standard Classified Nomenclature in every regard. There is no need in a hospital morbidity list of special entries for torticollis or for menopause or cretinism or idiocy and many other conditions rarely encountered in general hospitals. The Welfare Council grouping follows neither the International List nor the Standard Classified Nomenclature. Only five of the groups are based on the principle of etiology; the others refer to symptomatology or anatomic site. This was due to the need for tabulating poorly recorded information. Until the Standard Classified Nomenclature becomes generally used, a compromise arrangement must be worked out.

The four considerations followed in the tabulation of the material by the Welfare Council of New York City should be critically reviewed and such changes suggested as would be most acceptable for general adoption. The four guiding principles in the arrangement of the material were as follows:

1. Elimination of superfluous diagnostic notations. In the actual tabulation of the 576,000 hospital discharge records, a single diagnosis was chosen for 78 per cent of the cases, two diagnoses were entered in 17 per cent, three diagnoses in 4 per cent and in only 1 per cent of the cases were four diagnoses tabulated.

2. The discarding of complicating conditions which more or less regularly accompany the major condition or of typically secondary conditions.

3. The placement of several manifestations of the same etiology under one diagnostic designation.

4. Elimination of accessory conditions which are accidental and have no relation to the disease for which the patient was hospitalized.

Neither the Mayo Clinic nor the Welfare Council classification lists surgical operations. From an administrative as well as a social point of view it is desirable that hospital reports include a classification of operations, prepared in accordance with some uniform method to be agreed on.

There are numerous other tabulations of administrative value which should be correlated with the medical and surgical experience of the hospitals, such as total days' stay, the mortality, occupations and the seasonal cycle. I would like to emphasize several points in relation to hospital morbidity statistics:

1. A uniform classification of hospital morbidity and of surgical operations for comparative purposes is desirable.

2. It should be recognized that mass hospital statistics are of limited value from a clinical point of view and that they are scientific only in a sense that they are carefully prepared and correlated in accordance with certain agreed on principles of sound statistical procedure.

3. The availability of the Standard Classified Nomenclature is a factor in making such tabulations easily referable to accurate clinical entries and simplifies the work of coding.

4. Hospital morbidity statistics should be prepared in close conformity with the International List of Causes of Death, because of convenience and cross reference.

Punch Cards and Tabulating Methods as Applied to Morbidity Reports

MRS. STELLA F. WALKER, Chicago: A punched card system may be planned to aid in the compilation of annual reports and periodic reports to the administrative and medical staffs, to supplement or replace indexes of diagnoses and operations, to make it possible to select one or more cases having certain combinations of information wanted for research purposes and to provide flexibility of analysis to keep pace with new developments in the medical field.

One can employ cards of different styles, various kinds of key punch machines, different styles of sorters and mechanical tabulators. Combinations can be made in a variety of patterns. A coded nomenclature of diagnoses and other codes must, however, be adopted. Selections cannot be made blindly, and one must consider personnel, cost of equipment and available room.

Every doctor wants certain data on the card, and his cooperation is the most essential element in the entire program. There are no perfect classifications or fixed codes; changes must be made to keep pace with progress.

At the Cook County Hospital, Chicago, the Standard Nomenclature was adopted in 1937 before the punched card system was installed. The eighty column card was selected. This

was started in May 1938, and was carried forward by the regular staff and backward through 1937 by WPA workers. It has been used on some 200,000 records. A small electrical key punch is used, and a sorter with a card counter attached and a multiple brush which makes it possible to select a long code of six places at one operation. Cards bearing a Standard Nomenclature code of five places, such as 23513 Head of femur, can be obtained by putting the cards through the machine once. This smaller group of cards can then be put through, with the multiple brush set to select all fracture codes: -416, -417, and -418. This short cut makes it unnecessary for us to maintain a file of diagnostic indexes in addition to the punched card. We have a file of case histories, a card file of patient name cards, and the punched cards.

With this system, if a doctor comes in and asks "If some one had one or two fingers cut off, does he ever develop urticaria?" I could say "If you had such a case and put it on the record, we could find it." The doctor thus feels a new respect for his new ideas and a new incentive to get things in the record when he sees them.

Are the Standard Nomenclature codes too long and cumbersome for punched card use? A shorter code would be preferable provided it told as much and was as flexible in the making of new codes. The topographic code linked with an etiologic code has many advantages in flexibility of analysis. Perhaps this is particularly true at the County Hospital, where we have a general hospital and psychopathic, pediatric, tuberculosis and contagious disease hospitals, and departments in the surgical specialties large enough to be compared with special hospitals.

We do not use mechanical tabulation. If tabulation is an important consideration, I believe that an abbreviated code such as that of the International List of Causes of Death or the Classified List recently furnished by the Research Bureau of the Welfare Council of New York City could be advantageously associated with the Standard Nomenclature.

After a patient enters the County Hospital it may require quite a list of codes to describe his condition, but provision is made for punching only three diagnoses on a card. The three that are most interesting from the standpoint of diagnosis and treatment given are selected. If there are more than three a number is punched indicating that fact, and the additional codes are written on the back of the card. These diagnoses are included in reviews by hand analysis.

The three diagnoses use thirty-six columns on the card. Part 2 of the card, consisting of eighteen columns, accommodates the information for the general code, such as service and attending doctor to whom patient was assigned, the patient's age, sex, color or race, nativity, occupation, present address, date of discharge, length of stay and the result.

There are twenty-six columns allowed for special codes, providing flexibility for special detail in different departments. The obstetric department has a code of its own, the ophthalmologic department another. In surgery we have made use of the coding as given in the New York Hospital Classified Nomenclature of Operations.

These codes form an important part of our system. It is the way around the bottleneck which stops many punched card systems from coming through on schedule. These codes are not at all alike—they don't have to be. Some of the most useful codes are the shortest. Our analysis sheets are simple. We will use a peg board spread—a perpetual inventory, growing month by month, service by service, into an annual report.

The punched card system was made for the hospital and not the hospital to produce a model punched card system. The punched card furnishes an index and a summary, not a complete case history.

Massachusetts Experience in Reporting Mental Disorders

DR. NEIL A. DAYTON, Boston: Since 1928 we have had in operation a centralized statistical system in Massachusetts. A new statistical system was written at that time, and installed in the sixteen mental hospitals and state schools under the department. A central training course was held for the various clerks. They were taken to a central institution in the middle of the state. A week's work was given them, working with actual case records, and then they went back to their institutions and started the use of the system. We had two clerks informed in every institution as to the method of carrying out the work. We have thirteen mental hospitals, three state schools for mental defectives, the mental wards of the state formerly at Tewksbury, the criminal hospital for the criminally insane, two veterans' hospitals and one large private hospital, McLean, under our system. All of them are sending cards in a routine manner to the department to cover every admission, discharge and death throughout the year. Our system is a three card system. The first card indicates the patient admitted to the hospital or in residence; the second card, not in residence but on the books. The third card means separation from the system as a whole, through discharge or death. We have a large master file in the central department which contains statistical cards on all patients admitted or discharged from our mental hospital. It is possible in the central department to go to the file and find the record of any patient who has been in any of our mental hospitals back to 1889.

In making up codes for research projects there is always a temptation to use a printed code and not operate directly to a card. I think this is by far the simplest method. In this instance the clerk takes the case record folder, sits down with the record, takes one of these cards and circles the information on the card. There is no writing, no coding to be done other than this. The material on this card, if written out, takes about two and one-half typewritten pages. The operator of the punching machine sets the circled card right on top of the magazine and punches the card directly from the circled card. Then when she runs the cards through the machine she holds the punched card up to the circled card before a strong light and by looking through she has an instant check on the card. If any of the circled portions of the circled card do not correspond to the punched card, it can be seen by holding the card up to a strong light. It obviates the necessity of punching a card a second time for a check on the punch method. The operators are fast. They can go through a card in ten or twelve seconds.

We have in the psychiatric classification a condensed classification. We had 150 items and we have reduced them to twenty-six. We set up this condensed classification and then give the detail in the second column. One would be circled for schizophrenia; the designation simple, hebephrenic, catatonic, paranoid and others would be circled 1, 2, 3, 4 or 5 in the second column. When the statistics are made up at the end of the year, it means a sorting on a single column and not a sorting on a number of columns.

We have many demands in the department for the names of patients coming under certain diagnostic classifications. For instance, some one wants to conduct a study on hebephrenia and he will ask "How many patients have you in all your institutions?" The system now involves twenty-one different institutions, and using the alphabetical index we can send the list back to the institution, arranged in alphabetical order. We use two blank spaces on the discharge card to record data that would not be on the admission card. This is the form of discharge, whether or not the patient was discharged from hospital, discharged from the physician, discharged from family care, discharged from escape, or cause of death on any of those items.

Our centralized statistical system takes all of the statistics out of the institutions and places them in a centralized location. It is a function now of the central department and not of the individual institutions. We have been able to work out the methodology, so there can be no variation between institutions. Everything is carried out in the same way in every institution. We have conferences every now and then for the statistical clerks, in which we iron out common problems. By taking the work out of the institutions and making it a central function, we avoid the unnecessary duplication of the institution making up an annual report and then the central department making up an annual report. When we have completed the institutional reports for the twenty-one institutions we combine them into the large report of the department of mental health, which is a volume of some 500 pages and involves 289 tables on admissions, discharges, deaths and resident population. The patients discharged from our mental hospitals last year had remained in the hospital an average of nine months. The patients who died

in the hospital had been there for an average of five and one half years. All patients leaving hospitals had been there an average of one year and nine months.

We are also able to provide immediate information on the hospital turnover without waiting to the end of the hospital year. At present we have a monthly report that comes back from our superintendents, from which we make up comparative statistics. We are continually getting requests from the Department of Public Welfare and interested agencies as to statistics on mental disease, and this gives us a way of answering these questions without having to wait until the end of the year. The card coming in from the institution is sent in thirty days after the patient is admitted. We give that interval because of the necessity for a complete history of mental disorders. All discharges and deaths come in within five days.

DISCUSSION

CHAIRMAN EMERSON: Dr. Dayton can you tell us how far you used the Standard Classified Nomenclature in elaborating your twenty-six categories of disease under which you classify your cases?

DR. NEIL A. DAYTON, Boston: We followed the Standard Nomenclature exactly. We have all the items that are used in the Nomenclature, but we have a condensation. For example, in schizophrenia there is one general heading of schizophrenia. Under that are assigned five or six different numbers of the Nomenclature. We have the schizophrenic in the first column. In the second we have the additional numbers for the others. So we have the complete Nomenclature, but it is used in that condensed form.

(To be continued)

REGULATION OF THE SALE OF BARBITURATES BY STATUTE

PREPARED BY THE BUREAU OF LEGAL MEDICINE AND LEGISLATION, AMERICAN MEDICAL ASSOCIATION

Twenty-seven states have enacted laws, as of May 1, 1940, regulating the sale of barbiturates.[1] In all but one of these states, retail sales of such drugs to consumers may be made only on prescription. In Oklahoma, such sales may be made either on prescription or without a prescription if the pharmacist records the sale in much the same manner as he is required to record sales of poisons generally.

The laws that have been enacted follow no well defined pattern with respect either to the framework of the law or to the drugs included. In four states[2] the regulation of the sale of barbiturates is accomplished through the medium of food, drug and cosmetic acts. In two other states[3] such drugs are brought within the purview of narcotic drug acts. With respect to the coverage of the several laws there is a wide divergence. The laws do not all limit the included drugs to barbiturates, a number of states including other hypnotic or somnifacient drugs. A panoramic picture of the situation in this respect is presented by the following list of drugs included in one or more of the twenty-seven state laws. The names of the drugs are reproduced as they appear in the laws and without regard to approved terminology:

Allonal
Amytal
Barbital
Barbituric acid (malonylurea)
Diethylbarbituric acid
Ipral
Luminal
Medinal
Neonal (soneryl)
Noctal
Phanodorn
Phenobarbital
Proponal
Sandoptal
Veronal (barbitone)
Carbromal
Chloral (chloral hydrate)
Chlorbutanol
Diethylsulphon diethylmethane (Tetronal)
Sulphonethylmethane (trional)
Sulphonmethane (sulphonal)

In practically all of the states compounds, derivatives and preparations of the included drugs are covered.

Compounds, derivatives and preparations intended for external application, such as gargles, sprays or liniments, are specifically excluded, subject to certain restrictions, from the proscriptions contained in the laws of seven states.[4]

In ten states the laws definitely either forbid the refilling of prescriptions[5] or provide that they may be refilled only on the direction of the prescriber.[6] In New York, by a rule of the board of Regents of the University of New York, no prescription for a hypnotic or somnifacient drug intended for internal use may be refilled if it bears the statement of the prescriber that it is not to be refilled. In two states that otherwise forbid the refilling of prescriptions except on the written order of the prescriber, prescriptions for phenobarbital may be refilled without such written order.[7] In one state, Virginia, the law definitely says that a prescription may be refilled. In the other states the laws contain no express provision with respect to the refillability of prescriptions.

The provisions of the laws that have been enacted to date with respect to the drugs included, the limitations imposed on their sale, the records to be kept, and the labeling requirements are abstracted in the analysis that follows. The phrase "included drugs" as used in the analysis refers to the drugs that are covered in the particular law. In some of the laws reference will be found to a requirement imposing on pharmacists a duty to retain prescriptions for barbiturates or other included drugs in their files for a definite period of time. The absence of such a reference in other laws does not necessarily mean that there is no such requirement in those states, because there may be a general law imposing the requirement with respect to all prescriptions. The analysis follows:

Alabama

1. Citation: Laws of Alabama, 1935, Act No. 236.

2. Drugs Included: "Barbital, sulphonethylmethane (trional), sulphonmethane (sulphonal), diethylsulphon diethylmethane (tetronal), paraldehyde and chloral or chloral hydrate or any derivatives, compounds or mixtures of any of the drugs possessing hypnotic properties or effects."

3. Limitations on Sales: Included drugs may not be sold, furnished or given away except on the "original written order or prescription of a lawfully authorized practitioner of medicine." The law does not indicate whether or not a prescription may be refilled.

4. Records: The law contains no requirement as to the keeping of records of sales.

5. Labeling Requirements: The law does not specify that containers of any of the drugs must bear any label.

Arkansas

1. Citation: Laws of Arkansas, 1935, Ch. 113 and Ch. 327.

2. Drugs Included: "Barbituric acid or derivatives and compounds thereof under any copyrighted or chemical name."

3. Limitations on Sales: Included drugs may not be sold except on the prescription of a "legally qualified physician or by a legally qualified dispensing physician." Excepted from this restriction are sales by manufacturers or chemical houses to wholesale drug houses or to hospitals or retail pharmacies or by wholesale drug houses to hospitals or to retail pharmacies. No prescription may be refilled.

4. Records: Orders "by the retail pharmacy or hospital or dispensing physician, dentist or veterinarian" from wholesale drug houses, chemical houses or manufacturers must be in writing, in triplicate, one copy given to the seller, one copy to the food and drug division of the state board of health, and the original copy retained by the purchaser. The orders must be preserved for at least two years by the wholesale drug houses, chemical houses or the manufacturer or pharmacy or hospital, subject to inspection by any officer of the state board

1. Alabama, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Maine, Maryland, Minnesota, Mississippi, Nebraska, Nevada, New Jersey, New York, North Carolina, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Tennessee, Vermont, Virginia, Washington and West Virginia.
2. Connecticut, Florida, Nevada, North Carolina.
3. Vermont, West Virginia.
4. Colorado, Nebraska, New Jersey, New York, Oklahoma, Rhode Island, Vermont.
5. Arkansas, Colorado and Mississippi.
6. California, Minnesota, Nebraska, Oklahoma, Oregon, Vermont, Washington.
7. California and Oregon.

of health. A dispensing pharmacist must keep all prescriptions for any of the included drugs in a separate file for at least two years, subject to inspection by any officer of the law or by any inspector of the state board of health.

5. Labeling Requirements: The law does not require that containers of any of the included drugs must be labeled in any particular manner.

California

1. Citation: Laws of California, 1931, Ch. 249.

2. Drugs Included: "Veronal, barbital (acid diethylbarbituric) or any of its salts, derivatives, or compounds of the foregoing substance, or any preparation or compound containing any of the foregoing substance, or its salts, derivatives or compounds, or any registered, trade-marked or copyrighted preparation or compound registered in the United States patent office containing more than forty (40) grains to the avoirdupois or fluid ounce of the above substance."

3. Limitations on Sales: No person may sell, furnish or give away or offer to sell, furnish or give away any of the included drugs, "except upon the written order or prescription of a physician and surgeon, dentist or veterinary surgeon duly licensed to practice in the State of California." The law does not apply to sales at wholesale by drug jobbers, drug wholesalers and drug manufacturers to pharmacies or to physicians, dentists or veterinary surgeons, "nor to each other, nor to the sale at retail in pharmacies by pharmacists to each other or to physicians and surgeons, dentists or veterinary surgeons duly licensed to practice" in California. No prescription may be refilled "without the written order of the prescriber," except that any prescription for phenobarbital or any preparation, mixture or compound of phenobarbital may be refilled without such written order.

4. Records: A prescription or order must be preserved for at least three years from the date of filing and must be open at all times to inspection by duly authorized officers of the law.

5. Labeling Requirements: The law contains no requirement that containers of any of the included drugs must bear any particular type of label.

Colorado

1. Citation: Laws of Colorado, 1935, Ch. 106.

2. Drugs Included: "Salts of barbituric acid also known as malonylurea," "sulphonethylmethane (trional) or sulphonmethane (sulphonal) or diethylsulphon diethylmethane (tetronal) or carbromal, by whatever name they may be known, or paraldehyde," and chloral or chloral hydrate, or any derivative, compound or mixture or preparation thereof possessing hypnotic properties or effects. The law includes the foregoing drugs only when used internally. Expressly excluded are sprays, gargles and liniments if used externally and all compounds, mixtures or preparations intended for external use if they are sold in good faith and contain other drug or drugs conferring medicinal qualities.

3. Limitations on Sales: The law prohibits the sale or dispensing at retail of any of the included drugs except on a written prescription of a duly licensed physician, dentist or veterinarian. Only "one sale" may be made on each prescription. The law specifically excepts from its provisions dispensing by a duly licensed physician, dentist or veterinarian to patients "under their immediate supervision." A prescription may not be refilled.

4. Records: The law does not specify that records must be kept of the sale of any of the included drugs.

5. Labeling Requirements: A pharmacist must place on the container of a dispensed drug a label bearing his name and address, the date the prescription was compounded, the consecutive number of the prescription, the name of the prescribing "physician, dentist or veterinarian," and directions for use as given on the prescription. Manufacturers, jobbers, pharmacists or other dealers in any of the included drugs must keep such drugs in a container, the label of which must contain conspicuously in printed words the specific name of the drug and the proportion or amount thereof in the container.

Connecticut

1. Citation: Laws of Connecticut, 1939, Ch. 364.

(In Connecticut, the Food, Drugs and Cosmetic Act declares a drug to be misbranded if it is a drug sold at retail for use by man and contains any quantity of barbituric acid or any derivative thereof, unless it is sold on a written prescription signed by a member of the "medical, dental or veterinary profession who is licensed by law to administer such drugs, and its label shall bear the name and place of business of the seller, the serial number and date of such prescription and the name of such member of the medical, dental or veterinary profession.")

Delaware

1. Citation: Laws of Delaware, 1939, Ch. 92.

2. Drugs Included: Barbital, which is defined to mean "the salts of barbituric acid, also known as malonylurea, or any derivative or compound or any preparations or mixtures thereof containing more than ten grains to the avoirdupois or fluid ounce of the said substance," and other hypnotic or somnifacient drugs, defined to mean "sulphonethylmethane (trional) or sulphonmethane (sulphonal) or diethylsulphone diethylmethane (tetronal), or paraldehyde or any derivative or compound, or any preparation or mixture containing more than ten grains to the avoirdupois or fluid ounce of the said substances and chloral or chloral hydrates, or chlorbutanol, or any compounds or mixtures thereof containing more than ten grains to the avoirdupois or fluid ounce of the said substances when such chloral or chloral hydrates or chlorbutanol, or compounds or mixtures thereof are to be used internally." The law applies also to any of the substances specified by whatever name they may be known.

3. Limitations on Sales: No included drugs may be sold at retail or dispensed to any person except on the written prescription of a duly licensed physician, dentist or veterinarian, the term "physician" being defined to mean any duly licensed physician of any school of practice. The law contains no prohibition against the refilling of a prescription but imposes on every pharmacist, physician, dentist, veterinarian or licensed jobber dispensing any of the drugs the duty of keeping an accurate record "of all renewals."

4. Records: Pharmacists, physicians, dentists, veterinarians and licensed jobbers must keep a record of the name and address of the patient for whom the drug is prescribed, the date and the name and quantity of the drug dispensed, and an accurate record of all "renewals."

5. Labeling Requirements: A pharmacist who sells any of the included drugs on prescription must attach a label to the container bearing the name and address of the pharmacist, the date compounded and the consecutive number of the prescription under which it is recorded in his files, the name of the physician, dentist or veterinarian who prescribed the drug, and the directions for the use of the drug as given on the prescription. Manufacturers, pharmacists, jobbers or other dealers must place on the container of any included drug a label stating conspicuously in printed words the specific name of the drug and the proportion or amount in the container, such label being not required when the drug is dispensed by a pharmacist on a prescription and the container is labeled in the manner described.

Florida

1. Citation: Laws of Florida, 1939, Ch. 19656.

(The Food, Drug and Cosmetic Act of Florida declares a drug to be misbranded if it is a drug sold at retail for use by man and contains any quantity of barbituric acid, unless it is sold on a written prescription signed by a member of the medical, dental or veterinary profession who is licensed by law to administer such drugs, and its label bears the name and place of business of the seller, the serial number and date of the prescription, and the name of such member of the medical, dental or veterinary profession.)

Georgia

1. Citation: Laws of Georgia, 1939, Act No. 184.

2. Drugs Included: "Amytal, luminal, veronal, barbital, acid diethylbarbituric, sulfanilamide, prontylin, neo-prontosil, or any

salts, derivatives or compound of the foregoing substances, or their salts, derivatives or compounds or any trade marked or copyrighted preparation or compound registered in the United States Patent Office containing more than four (4) grains to the avoirdupois or fluid ounce of the above substances."

3. Limitations on Sales: No person, firm or corporation or association may sell, give away, barter, exchange, distribute or possess any of the included drugs except on a prescription of a duly licensed physician, the term "physician" being defined to mean a person authorized by the laws of Georgia to practice medicine and any other person authorized by law to treat sick and injured human beings and animals in the state and to use, mix, prepare, dispense and administer drugs in connection with such treatment. Excepted from the law are sales at wholesale of any of the included drugs by recognized drug jobbers or wholesalers and drug manufacturers to pharmacists or drug stores or to physicians qualified to practice their profession according to law, and sales by pharmacists in drug stores to one another. The law apparently places no restriction on the refilling of a prescription.

4. Records: The law does not require that records be kept of sales.

5. Labeling Requirements: A pharmacist who dispenses any of the included drugs is required to write on the container thereof the name of the patient, the name of the physician prescribing the drug, the name and address of the drug store or pharmacy from which the drug is dispensed, and the date of the prescription. A physician who dispenses any of the included drugs is required similarly to label the containers of the drugs.

Maine

1. Citation: Laws of Maine, 1933, Ch. 204; Laws of 1939, Ch. 209.

2. Drugs Included: "Veronal or barbital or any other salts, derivatives or compounds of barbituric acid or any registered, trade-marked or copyrighted preparation registered in the United States Patent Office containing the above substance."

The board of registration in pharmacy is authorized by regulation to designate as "potent medicinal substances, any compounds of barbituric acid, which are likely to be injurious to health if improperly used, and it shall be unlawful for any person, firm or corporation to sell, furnish or give away, or to offer to sell, furnish or give away any of such potent medicinal substances so designated," except under the conditions set forth in section 3 of this analysis.

3. Limitations on Sales: No person, firm or corporation may sell, furnish or give away, or offer to sell, furnish or give away any of the included drugs except on the written order or prescription of a physician and surgeon, dentist or veterinary surgeon. The proscription does not apply to sales at wholesale by drug jobbers, drug wholesalers and drug manufacturers to registered pharmacists and pharmacies, physicians, dentists, veterinary surgeons, hospitals, registered nurses, "nor to each other." Neither does the act apply to retail sales in pharmacies by pharmacists to each other, to physicians and surgeons, to dentists, veterinary surgeons, hospitals or registered nurses. The law specifically provides that nothing in it shall be construed to affect the right of a "physician and surgeon, dentist, veterinary surgeon or registered nurse in good faith and in the legitimate practice of his profession personally to administer, prescribe or deliver any of the foregoing substances." There is no prohibition against the refilling of prescriptions.

4. Records: The law imposes no requirement with respect to the keeping of records of sales.

5. Labeling Requirements: There is no provision in the law relating to the labeling of containers of included drugs.

Maryland

1. Citation: Laws of Maryland, 1935, Ch. 172; Laws of 1937, Ch. 237.

2. Drugs Included: Barbital, defined to mean "the salts of barbituric acid, also known as malonylurea, or any derivative or compounds or any preparations or mixtures thereof." The law also embraces other hypnotic or somnifacient drugs, defined to mean "sulphonethylmenthane (Trional) or sulphonmethane (Sulphonal) or diethyl-sulphone, diethyl-methane (Tetronal), or paraldehyde or any derivatives or compounds or any preparations or mixtures thereof and chloral or chloral hydrate, or chlorbutanol or any compounds or mixtures thereof when such chloral or chloral hydrate or chlorbutanol or compounds or mixtures thereof are to be used internally." It is further provided that the law shall apply "to any of the above mentioned drugs, or any derivatives or compounds or any preparations or mixtures thereof, as above set forth, whatever may be the name under or by which the same may be called or known."

3. Limitations on Sales: No included drug may be sold at retail or dispensed to any person in Maryland except on the written prescription of a duly licensed physician, dentist or veterinarian. The proscription does not apply to the administering or dispensing of included drugs by duly licensed physicians, dentists or veterinarians to bona fide patients when administered or dispensed in good faith. The law does not indicate whether a prescription may or may not be refilled.

4. Records: There is no specific requirement as to the keeping of records of sales.

5. Labeling Requirements: A pharmacist must affix a label on containers of drugs dispensed on prescription, bearing the name and address of the pharmacist, the date the prescription was compounded, the consecutive number of the prescription in the pharmacist's file, the name of the prescriber and directions for use as given on the prescription. A manufacturer, pharmacist, jobber or other dealer in drugs must affix a label on the container of such drugs, stating conspicuously in printed words the specific name of the drug and the proportion or amount thereof, such label being unnecessary when the drug is dispensed by a pharmacist on a prescription and the container is labeled in the manner indicated in the preceding sentence.

Minnesota

1. Citation: Laws of Minnesota, 1939, Ch. 102 and Ch. 193.

2. Drugs Included: Barbital, defined to mean "barbital and any derivative thereof; diethylbarbituric acid; any alkyl, aryl, metallic or halogenated derivative of barbituric acid; veronal (barbitone); proponal; ipral; neonal (soneryl); sandoptal; amytal; phenobarbital (luminal); phanodorn; noctal; allonal (which contains allylisopropyl-barbituric acid in combination with amidopyrine); medinal; any preparation, mixture or other substance containing any of the foregoing substances."

3. Limitations on Sales: No person, firm or corporation may sell, give away, barter, exchange or distribute barbital, except on a written prescription of a doctor of medicine, doctor of dental surgery or doctor of veterinary medicine, lawfully practicing his profession in Minnesota. The law does not apply to sales by wholesale drug concerns, registered pharmacies, licensed pharmacists, doctors of medicine, doctors of dentistry, doctors of veterinary medicine, or any bona fide hospital or other bona fide institutions wherein sick and injured persons are cared for or treated, or bona fide hospitals where animals are treated. The law further provides that a licensed doctor of medicine, or a licensed doctor of dentistry, in good faith and in the course of his professional practice only, may prescribe, administer and dispense barbital, or he may cause the same to be administered by a nurse or intern under his direction and supervision. The written or verbal consent of the prescriber is necessary to legalize the refilling of a prescription and if the consent is verbal it must be given directly from the prescriber to the pharmacist who refills. The pharmacist must note in ink or indelible pencil on the original prescription the date of the consent and the name of the pharmacist.

The law further provides that a licensed doctor of veterinary medicine, in good faith and in the course of his professional practice only, and not for use by a human being, may prescribe, administer and dispense barbital, and he may cause the same to be administered by an assistant under his direction and supervision.

4. Records: The pharmacist must indicate, in ink, on the prescription the fact that it has been compounded and the date compounded and must retain the prescription in a separate file for at least two years open to the inspection of any officer on whom the duty devolves to enforce the act.

5. Labeling Requirements: The container of a drug dispensed on prescription must bear a label containing the directions specified on the prescription and must contain the following warning: "Use Only As Directed."

Mississippi

1. Citation: Laws of Mississippi, 1940. Ch. —— (H. Bill No. 150, approved March 22, 1940).

2. Drugs Included: "Barbituric acid and any compound, manufacture, salt, derivative mixture, or preparation of barbituric acid."

3. Limitations on Sales: Included drugs may not be sold, bartered or given away except on the written prescription of a physician, dentist or veterinarian, authorized by law to practice his profession and "possessing a current federal narcotic license." (A pending amendment proposes to substitute for the quoted phraseology the following: "duly registered with the Collector of Internal Revenue under the Harrison Act.") The law does not apply to sales by a wholesaler or manufacturer to any licensed dealer in the included drugs; to the "sampling" of such drugs to physicians, dentists or veterinarians by representatives of the manufacturer; nor to sales of "patent" or "common" medicines handled and sold by drugstores and commissaries, prepared and designated by reputable manufacturers for exclusive use in the treatment of sick mules, horses, cows, dogs, cats or other animals. No prescription may be refilled.

"Possession or custody" of included drugs by a physician, dentist or veterinarian, qualified as stated in section 2 of this analysis by representatives of manufacturers and by laboratories approved by the state board of pharmacy, is declared lawful. The use of such drugs for scientific and medical purposes and for purposes of instruction is expressly authorized.

4. Records: The law does not prescribe that records shall be kept of sales.

5. Labeling Requirements: The law contains no provision with respect to the labeling of containers of the included drugs.

Nebraska

1. Citation: Laws of Nebraska, 1935, Ch. 64.

2. Drugs Included: Barbital, defined to mean "the salts of barbituric acid also known as malonylurea, or any derivative or compounds or any preparations or mixtures thereof possessing hypnotic properties or effects." The law also includes other hypnotic or somnifacient drugs, defined to mean "sulphonethylmethane (trional) or sulphonmethane (sulphonal) or diethylsulphone diethylmethane (tetronal) or carbromal, or by whatever name they may be known, or paraldehyde or any derivatives or compounds or preparations or mixtures thereof possessing hypnotic properties or effects, and chloral or chloral hydrate or chlorbutanol or any compounds or mixtures thereof possessing hypnotic properties or effects, when such barbital or other hypnotic and somnifacient drugs, or any derivatives or compounds or mixtures or preparations thereof are to be used internally." Expressly excluded are compounds in which barbital, or derivatives thereof, are used for synergic action when the medicinal properties of the other drugs contained in the compound render it incapable of being used for its hypnotic properties or effects. Exempted from the provisions of the law also are compounds or mixtures or preparations intended to be used as a spray or a gargle or a liniment or in any other wise for external application, provided such compound, mixture or preparation contains, in addition to the content of barbital or other hypnotic or somnifacient drugs, some other drug or drugs conferring on it medicinal qualities other than those possessed by the barbital or other hypnotic or somnifacient drugs and that such compounds, mixtures or preparations are sold in good faith for the purpose for which they are intended and not for the purpose of evading the provisions of the law.

3. Limitations on Sales: No included drug may be sold at retail or dispensed to any person except on the written prescription of a duly licensed physician, dentist or veterinarian. The law does not prevent, however, retail sales to physicians, dentists or veterinarians for dispensing to their "patients," provided such sales are made on the signed order of such physician, dentist or veterinarian. Wholesale sales by manufacturers, pharmacists, jobbers or other dealers in drugs are not proscribed by the act. Furthermore, the provisions of the section limiting the sales of included drugs are specifically made inapplicable to "a duly licensed physician, dentist, or veterinarian, when in their judgment they deem it advisable to dispense any of the aforementioned drugs to their patients under their immediate supervision." No prescription may be refilled except on the written order of the duly licensed physician, dentist or veterinarian.

4. Records: The law imposes no requirement that records of sales be kept.

5. Labeling Requirements: A pharmacist must affix to the container of an included drug dispensed on a prescription a label bearing the name and address of the pharmacist, the date the prescription was compounded and the consecutive number of the prescription under which it is recorded in his prescription file, together with the name of the prescriber and the directions for the use of the drug as given on the prescription. No manufacturer, pharmacist or jobber or other dealer in drugs shall sell or have in his possession any included drug unless the container bears a label stating conspicuously in printed words the specific name of the drug and the proportion or amount thereof, such label not being necessary, however, when the drug is dispensed by a pharmacist on a prescription and the container is labeled in the manner described in the preceding sentence.

Nevada

1. Citation: Laws of Nevada, 1939, Ch. 177.

(The Food, Drug and Cosmetic Act of Nevada declares a drug to be misbranded if it is a drug sold at retail for use by man and contains any quantity of barbituric acid, unless it is sold on a written prescription signed by a member of the medical, dental or veterinary profession who is licensed by law to administer such drugs, and its label bears the name and place of business of the seller, the serial number and date of the prescription, and the name of such member of the medical, dental or veterinary profession.)

New Jersey

1. Citation: Laws of New Jersey, 1933, Ch. 279.

2. Drugs Included: Barbital, defined to mean "the salts of barbituric acid, also known as malonylurea, or any derivative or compounds, or any preparations or mixtures thereof possessing hypnotic properties or effects." The law also includes other hypnotic or somnifacient drugs, defined to mean "sulphonethylmethane (trional) or sulphonmethane (sulphonal) or diethyl sulphone diethylmethane (trional) or carbromal, by whatever name they may be known, or paraldehyde or any derivatives or compounds or preparations or mixtures thereof possessing hypnotic properties or effects, and chloral or chloral hydrate or chlorbutonol, or any compounds or mixtures thereof possessing hypnotic properties or effects, when such barbital or other hypnotic and somnifacient drugs, or any derivatives or compounds or mixtures or preparations thereof are to be used internally."

Specifically exempted are compounds, mixtures or preparations intended to be used as a spray or as a gargle or a liniment or in any wise for external application if they contain, in addition to the content of barbital or other hypnotic or somnifacient drug, some other drug or drugs conferring medicinal qualities other than those possessed by the barbital or other hypnotic or somnifacient drug, provided such compounds or mixtures or preparations are sold in good faith.

3. Limitations on Sales: No included drug may be sold at retail or dispensed to any person except on the written prescription of a duly licensed physician, dentist or veterinarian. The law does not apply to dispensing by physicians, dentists or veterinarians to patients under their immediate supervision, if the required records are kept. The law is silent with respect to the refillability of prescriptions.

4. Records: A physician, dentist or veterinarian who dispenses an included drug must keep a record of the date the drug is dispensed, the kind of drug, the quantity, and the name and address of the patient.

5. Labeling Requirements: A pharmacist must affix a label to the container of an included drug dispensed on prescription bearing the name and address of the pharmacist, the date the

prescription was compounded, the number of the prescription in the pharmacist's file, the name of the prescriber and directions for use as given on the prescription. No manufacturer, pharmacist, jobber or other dealer shall sell or have in his possession an included drug unless the container bears a label stating conspicuously in printed words the specific name of the drug and the proportion or amount thereof, such label not being necessary when the drug is dispensed by a pharmacist on a prescription and the container is labeled in the manner described in the preceding sentence.

New York

1. Citation: Laws of New York, 1939, Ch. 778.

2. Drugs Included: Barbital, defined to mean "the salts of barbituric acid, also known as malonylurea, or any derivative or compounds or any preparations or mixtures thereof possessing hypnotic properties or effects." The law also includes other hypnotic or somnifacient drugs, defined to mean and include "sulphonethylmethane (trional) or diethylsulphon diethylmethane (tetronal) or carbromal, by whatever name they may be known, or paraldehyde or any derivatives or compounds or preparations, or mixtures thereof possessing hypnotic properties or effects, and chloral or chloral hydrate or chlorbutanol or any compounds or mixtures or preparations thereof to be used internally." The law is inapplicable to any compound or mixture or preparation intended to be used as a spray or a gargle or a liniment or in any other wise for external application which contains, in addition to the included drug, some other drug or drugs conferring on it medicinal qualities other than those possessed by the included drug, and such compounds or mixtures or preparations are sold in good faith.

3. Limitations on Sales: No included drug may be sold at retail or dispensed to any person except on the written prescription of a duly licensed physician, dentist or veterinarian. The law does not apply to a duly licensed physician, dentist or veterinarian when in his judgment he deems it advisable to dispense any of the aforementioned drugs to his patients under his immediate supervision, provided the required records are kept. While the law itself contains no proscription on the refilling of a prescription, Rule 30 of the Board of Regents of the University of New York provides that no prescription for a hypnotic or somnifacient drug intended for internal use shall be refilled if it bears a statement by the prescriber that it is not to be refilled. (See *New York State Journal of Medicine*, Feb. 1, 1940, p. 156.)

4. Records: A licensed physician, dentist or veterinarian who dispenses an included drug must keep a record of the date he dispenses the drug, the name of the drug dispensed, the quantity and the name and address of the "patient."

5. Labeling Requirements: The container of an included drug dispensed on prescription must bear a label showing the name and address of the pharmacist, the date the prescription was compounded, and the consecutive number of the prescription under which it is recorded in the pharmacist's files, the name of the prescriber, and directions for use of the drug by the patient as given on the prescription. Manufacturers, pharmacists, jobbers or other dealers in drugs who sell other than on prescription must affix a label on the container stating conspicuously in printed words the specific name of the drug and the proportion or amount thereof in the container.

North Carolina

1. Citation: Laws of North Carolina, 1931, Ch. 162; Laws of 1939, Ch. 320.

(In 1939, a new Food, Drugs and Cosmetic Act was passed in North Carolina under which a drug is declared to be misbranded if it is a drug sold at retail for use by man and contains any quantity of barbituric acid, unless it is sold on a written prescription signed by a member of the medical, dental or veterinary profession who is licensed by law to administer such drug, and its label bears the name and place of business of the seller, the serial number and date of such prescription, and the name of such member of the medical, dental or veterinary profession. To the extent that this 1939 law regulates the sale of "barbituric acid" it apparently supersedes the earlier act passed in 1931, an analysis of which follows.)

2. Drugs Included: "Sulphonmethane (sulphonal); sulphonethylmethane (trional); diethyl sulphondiethylmethane (tetronal); diethyl barbituric acid (barbital); or any of the foregoing by whatsoever trade name or designation, or any compound, preparation, mixture or solution thereof, or any salt or derivative thereof or of barbituric acid possessing hypnotic properties or effects; chloral hydrate or any mixture or solution thereof containing twenty grains or more thereof to the fluid ounce."

3. Limitations on Sales: No included drug may be sold in quantities exceeding twelve therapeutic doses except to persons known to be suffering with epilepsy, the limitation not applying to prescriptions of duly licensed physicians, doctors of dental surgery or doctors of veterinary surgery. The law does not limit the sale of included drugs to nor dispensing by duly licensed physicians, doctors of dental surgery, or doctors of veterinary surgery lawfully practicing in the state, or to registered retail or wholesale pharmacists, or to hospitals and other institutions for the treatment of defective, afflicted, sick and injured persons. The law contains no restriction with respect to the refillability of prescriptions.

4. Records: Every person dispensing any included drug, other than on prescription, must record in a book kept for the purpose the name of the drug sold, the quantity delivered, the date of delivery, the name and address of the purchaser and the name of the dispenser, which record shall at all times be open to the inspection of the proper officer of the law.

5. Labeling Requirements: The law does not impose any requirement with respect to the labeling of containers of included drugs.

Oklahoma

1. Citation: Laws of Oklahoma, 1933, Ch. 77.

2. Drugs Included: "Veronal, barbital (acid diethylbarbituric), luminal, or any chloral hydrate, bromidia or any of the salts, derivatives, compounds, manufactures or mixtures of any of the foregoing substances, or any preparation or compound containing any of the foregoing substances or their salts, derivatives, manufactures or compounds, or any registered, trade marked, or copyrighted preparation or compound thereof registered in the U. S. Patent Office, containing more than ten grains of acid diethylbarbituric, or more than ten grains of chloral hydrate, in one fluid ounce, or, if a solid or semi-solid preparation in one avoirdupois ounce," except remedies, ointments or other preparations which are prepared for external use only.

3. Limitations on Sales: (*a*) It is declared unlawful for any pharmacist to sell to or any practitioner of medicine, osteopathy, or dentistry to prescribe any of the drugs listed under section 2 of this analysis, or somnos, for habitual users of such drugs. The law provides, however, that a lawfully authorized practitioner of medicine may prescribe in good faith for the use of any habitual user of "narcotic drugs" who is under his professional care such substances as he may deem necessary for their treatment when such prescriptions are not given for the purpose of evading the provisions of the law.

(*b*) No person, firm, corporation, copartnership or association may barter, sell, exchange, furnish or give away, or offer to barter, sell, exchange, furnish or give away any included drug except on the original written order or prescription of a lawfully authorized practitioner of medicine, osteopathy, dentistry or veterinary medicine, or, without such order or prescription, unless the pharmacist keeps a record of the sale as described under section 4 of this analysis.

(*c*) The restrictions as to sales do not apply to supplies and sales at wholesale by jobbers, wholesalers and manufacturers to legally licensed retail druggists or qualified physicians or to each other, nor to the sale at retail by retail druggists to regular practitioners of medicine, dentistry or veterinary medicine, nor to sales made to manufacturers of proprietary or pharmaceutic preparations for use in the manufacture of such preparations, nor to sales to hospitals, colleges, or scientific or public institutions.

A prescription may not be refilled except on the written order of the original prescriber for each and every subsequent compounding or dispensing and no copy or duplicate of such order or prescription may be made or delivered to any person.

4. Records: (*a*) As to prescriptions and orders, the law provides that they must be "permanently retained on file" by the person or firm dispensing or compounding and must always be open to inspection by the prescriber or by an authorized officer of the law. (*b*) As to drugs dispensed without a written order or prescription, the law provides that the pharmacist or "legally licensed dispenser of retail drugs" shall keep a written record of sales. The record of each sale must be signed by the purchaser and must contain a true statement showing (1) name, age and address of purchaser, (2) character of drug and quantity purchased, and (3) name and address of parent, guardian or nearest of kin of purchaser. A complete copy of this record must be filed with the county clerk on or before January 1 of each year and the county clerk must within ninety days of the receipt of such copy certify an abstract of it to the commissioner of public health. The commissioner is required to examine all such records and to make "a summary report thereon to the Fifteenth Session of the Legislature."

5. Labeling Requirements: The law imposes no requirements with respect to the labeling of containers of any included drug.

Oregon

1. Citation: Laws of Oregon, 1935, Ch. 203.

2. Drugs Included: "Amytal, luminal, veronal, barbital, acid diethylbarbituric, or any of its salts, derivatives, or compounds of the foregoing substance, or any preparation or compound containing any of the foregoing substance, or its salts, derivatives or compounds, or any registered, trademarked or copyrighted preparation or compound registered in the U. S. Patent Office containing more than four grains to the avoirdupois or fluid ounce of the above substance."

3. Limitations on Sales: No person, firm or corporation may sell, give away, barter, exchange or distribute any of the included drugs except on the written order or prescription of a physician and surgeon, dentist or veterinary surgeon duly licensed to practice in Oregon. The law does not apply to the sale at wholesale of any of the included drugs by drug jobbers, drug wholesalers and drug manufacturers, to pharmacies, or to physicians, dentists or veterinarians, nor to each other, nor to the sale at retail in pharmacies by pharmacists to each other or to physicians and surgeons, dentists or veterinary surgeons licensed to practice in the state. A prescription for phenobarbital or any preparation, mixture or compound of phenobarbital may be refilled. Prescriptions for other included drugs may not be refilled without the written order of the prescriber.

4. Records: A prescription or order shall be preserved for at least three years from the date of filling and must at all times be open to inspection by duly authorized officers of the law.

5. Labeling Requirements: The law contains no requirements with respect to labeling.

Pennsylvania

1. Citation: Laws of Pennsylvania, 1935, Act No. 407.

2. Drugs Included: The law covers "hypnotic drugs" and "other hypnotic drug or analgesic drug, or body weight reducing drug." The term "hypnotic drug" is defined to mean "drugs, known as barbital and the salts of barbituric acid, also known as malonylurea, or any derivative or compounds, or any preparations or mixtures thereof, possessing hypnotic properties or effects." The term "other hypnotic drug, or analgesic drug, or body weight reducing drug" is defined to mean "sulphonethylmethane (Trional), or sulphonmethane (Sulphonal), or diethylsulphon diethylmethane (Tetronal), or bromdiethyl acetylcarbamide (carbromal), by whatever name they may be known; or paraldehyde, or any derivatives or compounds or preparations or mixtures thereof, possessing hypnotic properties or effects; and chloral or chloralhydrate or chlorbutanol, or any compounds or mixtures thereof possessing hypnotic properties or effects; or phenylcinchoninic acid (cinchophen), an analgesic anti-rheumatic drug, or any derivative or compound including atophan and atoquinol or dinitrophenol, a metabolic accelerator body-weight reduction drug, or any dinitro compounds including dinitrophenol sodium, and dinitrocresol sodium, when the drugs herein defined or any derivatives or compounds or mixtures or preparations thereof." [This sentence is incomplete but it is quoted verbatim from the official laws of Pennsylvania.]

3. Limitations on Sales: No included drug may be sold at retail or dispensed to any person except on the written prescription of a duly licensed physician, dentist or veterinarian. This proscription does not apply to a duly licensed physician, dentist or veterinarian. The law contains no restriction with respect to the refillability of prescriptions.

4. Records: A physician, dentist and veterinarian must keep a record of the amount of included drugs purchased and a dispensing record showing the date, name of, the quantity of the drugs dispensed, and the name and address of the patient.

5. Labeling Requirements: (*a*) A physician, dentist or veterinarian must affix to the container of a drug sold or dispensed a label bearing the name and address of the dispenser, the date dispensed, the name and address of the patient, and the directions for the use of the drug by the patient. (*b*) A pharmacist must affix to the container of an included drug sold on prescription a label bearing the name and address of the pharmacist, the date compounded, and the consecutive number of the prescription under which it is recorded in his prescription files, together with the name of the physician, dentist or veterinarian prescribing it. (*c*) No manufacturer, pharmacist, jobber, dealer in drugs or any other person may sell or have in his possession any included drug unless the container bears a label stating conspicuously the specific name of the drug and the proportion or amount thereof, provided such label is not necessary when the drug is dispensed by a pharmacist on a prescription, or dispensed by a physician, dentist or veterinarian, and the container is labeled in the manner described.

Rhode Island

1. Citation: Public Laws of Rhode Island, 1937, Ch. 2543.

2. Drugs Included: Barbital, defined to mean "the salts of barbituric acid, also known as malonylurea, or any derivative or compounds or any preparations or mixtures thereof possessing hypnotic properties or effects." The law also includes "other hypnotic or somnifacient drug," defined to mean "sulphonethylmethane (trional) or sulphonmethane (sulphonal) or diethylsulphon diethylmethane (tetronal) or carbromal, by whatever name they may be known, or paraldehyde or any derivatives or compounds or preparations or mixtures thereof possessing hypnotic properties or effects, and chloral or chloral hydrate or chlorbutanol or any compounds or mixtures thereof possessing hypnotic properties or effects." The law applies to the foregoing drugs only when they are to be used internally, and specifically is excluded any compound or mixture or preparation that is intended to be used as a spray or a gargle or a liniment or in any other way for external application, provided that such compound mixture or preparation contains, in addition to the content of any of the included drugs, some other drug or drugs conferring on it medicinal qualities other than those possessed by the included drugs alone, provided such compounds or mixtures or preparations are sold in good faith.

3. Limitations on Sales: The included drugs may not be sold at retail or dispensed to any person except on the written prescription of a duly licensed physician, dentist or veterinarian. The proscription does not apply to a duly licensed physician, dentist or veterinarian when in his judgment it is advisable to dispense any of the drugs to a patient under his immediate supervision. The law contains no restriction with respect to the refillability of prescriptions.

4. Records: The law does not require that records be kept of sales.

5. Labeling Requirements: A label must be placed on the container of an included drug dispensed on prescription showing the name of the drug and the name and address of the seller. Manufacturers, wholesalers, jobbers, pharmacists and other dealers in drugs may not have in their possession any of the included drugs unless the container bears a label showing the specific name of the drug and the amount thereof,

except that such label is not necessary when the drug is dispensed by a pharmacist on a prescription and the container is labeled as indicated in the preceding sentence.

South Carolina

1. Citation: Laws of South Carolina, 1939, Governor's Act No. 514.

2. Drugs Included: The law embraces generally "that general class of synthetic drugs commonly known as barbiturates or their compounds." The law provides, however, that compounds containing not more than one fourth of the "standard dose" of a barbituric acid preparation which in combination with active medicinal ingredient or ingredients, the activity of which will preclude the use of the compound to obtain the full effect of the barbituric acid preparation shall be exempt from the provisions of this act. A "standard dose" is defined to be "such as is listed in the 'Pharmacopoeia,' and, if not listed in the 'Pharmacopoeia,' then as listed in the book 'New and Nonofficial Remedies,' and if not listed in either the 'Pharmacopoeia' or the 'New and Nonofficial Remedies,' then a standard dose shall be the average dose recommended by the manufacturer of the compound."

3. Limitations on Sales: No person, firm or corporation may sell, barter, exchange or give away any of the included drugs except on the written prescription of a licensed physician, or the prescription of a person authorized to prescribe narcotic drugs. The law is inapplicable to the sale, barter, exchange or giving away of any of the included drugs to retail or wholesale druggists, licensed physicians, licensed dentists and licensed veterinarians, "without such written prescription." The law provides further that it is not to be construed to prohibit or limit licensed physicians, licensed dentists and licensed veterinarians from dispensing any of the included drugs in the regular course of their practice, provided "upon any such barbiturate or barbiturate compound being dispensed by a licensed physician, licensed dentist, or licensed veterinarian, so much of such barbiturate or barbiturate compound not to be consumed in the presence of such person so dispensing same shall be placed in a container in the manner as provided hereinabove." The law does not indicate whether or not a prescription may be refilled.

4. Records: Every person, firm or corporation selling, bartering, exchanging or giving away any of the included drugs on a written prescription must retain the prescription for a period of three years from the date of receiving it and must exhibit it to the state board of health, or any officer or employee thereof, on demand. Retail and wholesale druggists are required to submit to the state board of health at least once every twelve months a sworn statement showing the amount of included drugs received and disposed of by them during "some specified time," and such other information as the board may require.

5. Labeling Requirements: Every person dispensing an included drug on a prescription must place the drug "in a container with the name and address of the person prescribing same and the name and address of the person, firm or corporation dispensing same plainly printed or written thereon." A physician, dentist or veterinarian who dispenses to a patient any included drug to be consumed out of the presence of the physician, dentist or veterinarian must place the drug in a container as described in the preceding sentence.

Tennessee

1. Citation: Laws of Tennessee, 1939, Ch. 164.

2. Drugs Included: The law embraces "barbital," which is defined to mean "the salts of barbituric acid, also known as malonylurea, or any derivative or compounds or any preparations or mixtures thereof possessing hypnotic properties or effects."

3. Limitations on Sales: The law provides that no person, firm or corporation may sell, barter or give away any included drug except on the written prescription of a duly licensed physician, dentist or veterinarian. This proscription does not apply to sales by legitimate wholesale druggists to registered pharmacists and the sale by registered pharmacists to duly licensed physicians, dentists and veterinarians. The law does not indicate whether or not a written prescription may be refilled.

4. Records: The law does not require that any record be made of sales.

5. Labeling Requirements: No provision is contained in the law with respect to the labeling of containers of included drugs.

Vermont

1. Citation: Laws of Vermont, 1939, No. 128.

2. Drugs Included: The 1939 law amended the state narcotic act by including within its provisions "cincophen and compounds, amidopyrin, and compounds, such barbiturates as veronal, barbital, allonal, luminal, ipral and medinal or any other barbituric acid derivatives now available or such as may later be manufactured." The law provides that its provisions do not apply to liniments, ointments or other preparations which are prepared for external use only.

3. Limitations on Sales: The law provides that no person shall sell, furnish, give away or deliver any of the included drugs except on a prescription or order written by a licensed physician, dentist or veterinarian. It is expressly provided that the law shall not be construed to prevent a licensed physician, dentist or veterinarian from prescribing, administering or dispensing any drug that may be indicated for any patient under his care, if done in good faith. A veterinarian may not prescribe any of these drugs for the use of a human being. A prescription for any of the included drugs may not be refilled except on order of the prescriber.

4. Records: A prescription must show the date on which it is filled or refilled and must be retained on file by the druggist filling it for at least two years. The prescription may not be copied except for purpose of record by the druggist filling it and must at all times be open to inspection by members of the board of health, board of pharmacy, their authorized agents, and by the police authorities of the state.

5. Labeling Requirements: The law contains no provision with respect to the labeling of containers of any of the drugs named in section 2 of this analysis.

Virginia

1. Citation: Laws of Virginia, 1932, Ch. 377.

2. Drugs Included: The law includes hypnotic drugs, defined to mean "diethyl barbituric acid (barbital), by whatsoever trade name or designation; or any compound, preparation, mixture or solution thereof; or any salt or derivative thereof or of barbituric acid possessing hypnotic properties or effects."

3. Limitations on Sales: No person may sell or give away any included drug to a consumer except on a prescription of a doctor of medicine, doctor of dental surgery or doctor of veterinary surgery, lawfully practicing his profession. The law does not apply to sales to or the dispensing of such drugs by doctors of medicine, doctors of dental surgery or doctors of veterinary surgery, or sales to registered retail or wholesale pharmacists or hospitals, and other institutions for the treatment of defective, afflicted, sick and injured persons. A prescription "may be refilled."

4. Records: The law contains no provision with respect to the keeping of records of sales.

5. Labeling Requirements: The law contains none.

Washington

1. Citation: Laws of Washington, 1939, Ch. 6 and Ch. 29.

2. Drugs Included: The law embraces "amytal, luminal, veronal, barbital, acid diethylbarbituric, or any of their salts, derivatives, or compounds of the foregoing substances, or any preparation or compound containing any of the foregoing substances, or their salts, derivatives or compounds, or any registered, trade-marked or copyrighted preparation or compound registered in the U. S. patent office containing more than one grain to the avoirdupois or fluid ounce of the above substances," and "para-amino-benzene sulfonamide, sulfanilamid, sulfamidyl, prontylin, prontosil, neoprontosil, edimalin, sulfonamid or any salts, derivatives or compounds thereof or any registered, trade marked or copyrighted preparation or compounds registered in the U. S. patent office containing said substances."

3. Limitations on Sales: No person may sell, give away, barter, exchange or distribute any included drug except on the written order or prescription of a physician, surgeon, dentist or veterinary surgeon duly licensed to practice in Washington. The law does not apply to sales at wholesale by drug manufacturers, drug jobbers, and drug wholesalers to "pharmacies or to physicians, dentists, or veterinary surgeons, nor to each other, nor to the sale at retail in pharmacies by pharmacists to each other or to physicians, surgeons, dentists, veterinary surgeons duly licensed to practice in this state." A prescription may not be refilled except on the written order of the prescriber.

4. Records: The law does not require records to be kept of sales.

5. Labeling Requirements: The law contains none.

West Virginia

1. Citation: Laws of West Virginia, 1935, Ch. 46.

2. Drugs Included: The provisions here abstracted form a part of the state uniform narcotic act. They embrace "Chloral hydrate, or any compound, manufacture, mixture, or preparation thereof containing over two grains to the ounce," and "malonylurea (barbituric acid), as such, or diethyl-malonylurea, as such, or any sodium or potassium salt of either of them, under whatever name they may be designated, or any sodium or potassium salt of any chemical derivative of malonylurea, or diethyl-malonylurea, under whatever name they may be designated, that may be classed as a dangerous hypnotic or narcotic as defined by regulations of the state board of pharmacy."

3. Limitations on Sales: No person may sell or dispense at retail any included drug except on the written prescription of a physician, dentist or veterinarian. The law does not prevent the "supplying" of the drugs by a registered pharmacist to physicians, dentists, veterinarians and accredited hospitals for medicinal use. The law provides that a prescription for "narcotic drugs" may not be refilled; but since the law defines narcotic drugs to mean "coca leaves and opium," this proscription apparently does not apply to the drugs described in section 2 of this analysis.

4. Records: The law requires that certain records must be kept of sales of narcotic drugs but it is questionable whether this requirement is applicable to the sales of drugs described in section 2 of this analysis.

5. Labeling Requirements: The labeling requirements contained in the law relate to narcotic drugs.

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—A subcommittee of the House Committee on the Judiciary will hold a hearing, May 22, on H. R. 8963, the bill introduced by Representative Tolan, California, to give chiropractors the right to treat injured federal employees entitled to the benefits of the United States Employees' Compensation Act. Representative Francis E. Walter of Pennsylvania is the chairman of the subcommittee. The Senate Committee on Education and Labor scheduled a hearing on S. 3461 for May 13. This bill proposes to lodge with the United States Department of Labor supervision over industrial health by making available federal grants to states that have developed plans acceptable to the Secretary of Labor for the control and prevention of industrial conditions hazardous to the health of employees. On May 6 and May 10 the Senate Committee on Education and Labor conducted hearings on S. 3914, a bill introduced by Senator Pepper, Florida, to impose additional duties on the United States Public Health Service in connection with investigation and control of pneumonia, influenza and the common cold. S. 3633 has passed the Senate and House, providing that a candidate for appointment in the Dental Corps of the Army, to be eligible, must be a graduate of a recognized dental college, having been engaged in the practice of his profession for at least two years subsequent to graduation or, in lieu thereof, must have after such graduation satisfactorily completed a dental internship of not less than one year in a hospital or dispensary. S. 3654 has passed the House and Senate, increasing the authorized maximum number of enlisted men of the Medical Department of the Regular Army. H. R. 9236 has passed the House, proposing an additional appropriation of $75,000 for the preparation of "talking books" for the blind.

Bills Introduced.—H. R. 9537, introduced by Representative White, Ohio, proposes to amend the Fair Labor Standards Act of 1938 so as to exclude from its provisions relating to minimum wages and maximum hours students in recognized professional schools being given professional or clinical experience. S. 3924, introduced by Senator Wagner, New York, proposes to amend the Social Security Act so as to provide insurance benefits for wage earners permanently and totally disabled for causes not arising out of their employment. A copy of this bill is not yet available for analysis, but in submitting it to the Senate Senator Wagner said, in part: "Humanity and economy require that the disabled beneficiaries be restored to health in all cases where medical and surgical skill have progressed far enough to offer a remedy. The bill anticipates the need for rehabilitation, where such services may aid in restoring the beneficiary's working ability. The funds to be expended for the purpose of rehabilitation are carefully limited and could not be utilized for the construction of hospitals or other institutions." The bill was referred to the Senate Committee on Finance.

DISTRICT OF COLUMBIA

Change in Status.—H. R. 9525 has been reported to the House, with amendments, proposing to reorganize the government of the District of Columbia. The House Committee on the District of Columbia proposed no amendment to the bill with respect to the appointment of a health officer for the district. The committee did strike out the requirement that the chief medical examiner who is to direct the office of medical examiner of the District must be a doctor of medicine and in lieu thereof proposed that that official must be a "physician."

WOMAN'S AUXILIARY

California

Rabbi Edgar F. Magnin discussed "The Life of Alfred Adler," by Philip Bottome, before the auxiliary to the Los Angeles County Medical Association, January 23. More than 100 members were present. After the meeting the members viewed the Physicians' Art Exhibit.

The auxiliary to the Marin County Medical Society held a dinner meeting in Fairfax, January 25. Dr. Walter Brown, professor of public health at Stanford University, was speaker and Mrs. Brown and Mrs. Edmund Morrissey, president of the auxiliary to the San Francisco County Medical Society, were guests.

Indiana

Eleven auxiliaries to county medical societies were organized in Indiana during February, as follows: Grant, Marshall, Adams, Tippecanoe, Cass, Howard, Lake, Noble, LaGrange, Steuben and De Kalb.

The auxiliary to the Marion County Medical Society had an annual public relations tea at Indiana University Center, Indianapolis, March 4. Presidents of women's clubs of the county were special guests. Dr. Verne K. Harvey, director of the state board of health, outlined the various departments of the board and Dr. Herman G. Morgan, secretary of the city board of health, discussed "Modern Trends of Medicine."

The January meeting of the auxiliary to the Vigo County Medical Society was held in Terre Haute with fifty-seven in attendance. Miss Charlotte Lee, dramatic instructor at St. Mary's of the Woods School, read the play "No Time for Comedy." The auxiliary finances the occupational therapy work at St. Anthony's Hospital and at Union Hospital.

Iowa

The auxiliary to the Pottawattamie County Medical Society entertained the members of the society at a dinner at the home of Dr. and Mrs. Grant Augustine, Council Bluffs, February 26. Forty-two persons were in attendance and Mrs. A. A. Robertson was named president.

Louisiana

Dr. G. C. Anderson, president of the Orleans Parish Medical Society, spoke on the "Periodic Health Examination" at a meeting of the auxiliary to the Orleans Parish Medical Society, New Orleans, February 14.

Dr. Charles B. Odom, New Orleans, spoke on the Wagner Health Bill, February 13, at a public meeting in Opelousas, sponsored by the auxiliary to the St. Landry Parish Medical Society.

Michigan

At the February meeting of the auxiliary to the Genesee County Medical Society in Flint Mrs. Arthur Kretchmar spoke on "Six Years in Africa."

Dr. L. Fernald Foster discussed the Wagner Health Bill at the January meeting of the auxiliary to the Jackson County Medical Society.

The auxiliary to the Kalamazoo County Medical Society met January 16. "My Days of Strength," by Dr. Anne Walter Fearn, who spent forty-four years in China, was reviewed by Mrs. Walter den Bleyker.

The Monroe County Medical Society and its Auxiliary held a joint meeting in Monroe in February. Mr. Lee A. White of the Detroit *News* talked on "What Can We Believe?"

Minnesota

The midwinter meeting of the board of directors of the auxiliary to the Minnesota State Medical Association was held in Minneapolis January 23. Dr. E. L. Meyer showed motion pictures of South America and Dr. Bertram S. Adams, president of the Minnesota State Medical Association, was guest speaker.

New York

Mrs. Albert Vander Veer II, chairman of legislation of the auxiliary to the Medical Society of the State of New York, presented the content of bills affecting medical practice at the February meeting of the auxiliary to the Medical Society of Columbia County at the Hudson City Hospital in Hudson.

The auxiliary to the Cayuga County Medical Society is assisting in raising funds for the Physicians' Home and also assisting the medical society in raising funds to purchase cases for the Medical Historical Exhibit to be placed in the Cayuga Museum of History and Art.

South Carolina

The auxiliary to the Columbia Medical Society met in Columbia January 2, with fifty members in attendance. Dr. Roger Doughty spoke on socialized medicine.

The auxiliary to the Laurens County Medical Society met in Laurens February 26. Mrs. Mark S. Ellis spoke on "Emotional Development."

The auxiliary to the Oconee County Medical Society met in Seneca February 12. Mrs. William B. Furman, president of the auxiliary to the South Carolina Medical Association, was speaker and also read a paper entitled "Medicine Through the Ages."

Tennessee

The auxiliary to the Knox County Medical Society met in Knoxville March 6. Mrs. H. E. Christenberry reviewed the book "Centennial History of Tennessee State Medical Association."

Utah

The auxiliary to the Salt Lake County Medical Society met at the home of Mrs. John Z. Brown, Salt Lake City, January 15. "The Doctor's Wife," written by Dr. Rock Sleyster, President of the American Medical Association, was read.

Virginia

At the January meeting of the auxiliary to the Petersburg Medical Society, Mrs. Wright Clarkson reviewed "My Days of Strength," by Dr. Anne W. Fearn.

Dr. Walter B. Martin spoke on socialized medicine at a meeting of the auxiliary to the Norfolk County Medical Society in Norfolk January 30.

The auxiliary to the Mid-Tidewater Medical Society met in West Point January 24. An article, "Dollar-a-Month Doctor," by Lowell Lawrance, published in *Hygeia*, was read.

Washington

Dr. Joseph Low spoke on the Wagner Health Bill before the auxiliary to the Yakima County Medical Society January 8. Dr. Walter Cameron spoke on this bill before the auxiliary to the Pierce County Medical Society in Tacoma December 14. Dr. Helen Gibson Hogue, secretary of the Washington State Mental Hygiene Society, spoke on "Psychological Preparation for Living" before the auxiliary in Tacoma January 11.

The auxiliary to the Washington State Medical Association held its midyear board meeting in Tacoma February 16. Addresses were given by Drs. Warren B. Penney, president of the Washington State Medical Association; H. H. Skinner, chairman of Maternal and Child Welfare Committee, and A. J. Roth, member of the Health Education Survey of the State Planning Council.

The auxiliary to the Kitsap County Medical Society held its January meeting in Bremerton. State Senator Lulu Haddon, who is a member of the auxiliary, discussed the Wagner Health Bill. At a meeting of the auxiliary on March 15, Dr. Donald Trueblood, of Seattle, spoke on cancer.

The auxiliary to the Walla Walla Valley Medical Society met February 18. Rev. Joseph Settle, rector of St. Paul's Church, reviewed "As We Are," by E. F. Benson. At a meeting March 19, Richard Clodius, radio announcer, gave a talk on the history of broadcasting.

At a meeting of the auxiliary to the Grays Harbor County Medical Society in Hoquiam, February 21, Miss Elaine Hesla discussed "Wagnerian Opera."

The auxiliary to the King County Medical Society held its annual public relations dinner at the Women's University Club in Seattle, February 20. Several hundred guests attended. A discussion of medical affairs followed and questions were answered by members of the medical society.

"The Nation's Health," an editorial published in the February 1940 issue of *Hygeia*, was read and discussed at a meeting of the auxiliary to the Clark County Medical Society held at the home of Mrs. Charles Otto, near Vancouver, March 5.

The auxiliary to the Spokane County Medical Society met in Spokane February 9. Rev. Father James Linden, S.J., Regent of the School of Law of Gonzaga University of Spokane, spoke on the attitudes of Americans toward war, the third term and socialized medicine.

At a meeting of the auxiliary to the Spokane County Medical Society, March 8, Dr. Elizabeth White discussed the work of the Young Women's Christian Association. "At Miss Susie Slagle's," a novel by Augusta Tucker dealing with the lives of medical students in Baltimore, was reviewed by Mrs. Wesley H. DuBois.

West Virginia

The auxiliary to the Fayette County Medical Society met in Montgomery January 16. The address by Dr. Nathan B. Van Etten, delivered at White Sulphur Springs last July, was reviewed and discussed.

Mrs. J. Frank William Jr. spoke on "Medicine's Gift to Mankind" at a meeting of the auxiliary to the Harrison County Medical Society in Clarksburg February 1.

Dr. J. W. Davis spoke on "Community Interest in Health" at a meeting of the auxiliary to the Marion County Medical Society in Fairmont January 30.

Dr. Athey R. Lutz discussed "What Is Being Done for Crippled Children" at a meeting of the auxiliary to the Parkersburg Academy of Medicine February 14.

At a meeting of the auxiliary to the Raleigh County Medical Society in Beckley, January 29, Dr. Norman G. Patterson spoke on "Medicine in China."

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

Refresher Course on Pediatrics. — The third series of refresher courses sponsored by the committee on maternal and child welfare of the state medical society and the state board of health will be conducted during a six week period beginning May 20. Lectures on pediatric subjects will be given in Fort Smith, Prescott, McGehee, Searcy and Jonesboro. Dr. Jean Valjean Cooke, professor of obstetrics, Washington University School of Medicine, St. Louis, will be the speaker.

CALIFORNIA

Package Library.—The regents of the University of California have authorized an increase in the budget of the university's Medical Center Library in San Francisco to maintain a circulating periodical service for rural physicians throughout the state. The costs of this service will be for mailing only.

Physicians' Art Exhibit at Treasure Island. — The American Physicians' Art Association will conduct a free art exhibit in the Hall of Science Building, Treasure Island, San Francisco, from July 1 until the fair closes. The management of the fair has made available 2,976 square feet of floor space without charge to the association.

Society News.—Dr. Rudolf Schindler, Chicago, addressed a special meeting of the San Francisco County Medical Society, San Francisco, May 1, on "Gastric Carcinoma—Its Early Diagnosis and Prognosis." —— The California State Dental Association was addressed at its annual meeting in Oakland, May 14, by Dr. Edward C. Rosenow, Rochester, Minn., on "The Prevention and Elimination of Infections In and About Teeth and Thereby of Systemic Disease." Dr. Rosenow presented a "Review of Findings of the Los Angeles Poliomyelitis Epidemics of 1934 and 1937" before the Hollywood Academy of Medicine, May 9.

ILLINOIS

New Division of Cancer Control.—In accordance with recently enacted laws, a division of cancer control has been established in the state department of health with offices at 1800 West Fillmore Street, Chicago. Dr. Raymond V. Brokaw, New York, has been appointed chief of the division and Dr. Perry J. Melnick, Chicago, pathologist to supervise a diagnostic service. The total amount of funds available under the two laws is about $18,000 a year. The work will be largely educational, emphasizing early diagnosis and early scientific treatment of cancer. Laboratory diagnostic service will be provided to the extent of resources. Last year in Illinois 11,186 fatalities were attributed to cancer. The appointment of an advisory board to the division of cancer control has also been announced. Present members of the board include Drs. David J. Davis, dean of the University of Illinois College of Medicine, Chicago, chairman; James Scott Templeton, Pinckneyville; Roswell T. Pettit, Ottawa; William M. Cooley, Peoria, and Edwin F. Hirsch, Chicago, secretary.

Chicago

The Capps Prize.—The Institute of Medicine of Chicago announces that the 1939 award of the Joseph A. Capps Prize has been divided between Dr. Charles Fisher for his investigation on "Diabetes Insipidus and the Neurohormonal Control of Water Balance: A Contribution to the Structure and Function of the Hypothalamicohypophysial System," and Dr. Bernard G. Sarnat for his work on "The Teeth as Permanent Chronologic Recorders of Systemic Disease: A Clinical and Experimental Study of Enamel Hypoplasia."

The Bernard Fantus Clinics.—The new outpatient clinics of the Cook County Hospital group were dedicated, April 19, to the memory of the late Dr. Bernard M. Fantus, director of therapeutics at the county hospital and creator of the "blood bank" for quick transfusions, newspapers reported. All clinics of the hospital group except that for the obstetric ward, which will remain in its present quarters, will be housed in one building to bear the name of Dr. Fantus. The function of the new clinics will be to give follow-up treatment to county hospital patients.

INDIANA

District Meetings.—The First District Medical Society will be addressed, May 23, in Evansville by Dr. Homer G. Hamer, Indianapolis, on "Urinary Tract Infection and the General Practitioner."——The Second District Medical Society will be addressed in Sullivan, June 6, by Drs. Goethe Link and Ezra Vernon Hahn, Indianapolis, on "Surgical Management of Complicated Thyroid Conditions" and "Treatment of Brain Injury and Skull Fracture" respectively.——Dr. Winship C. Callaghan, Greensburg, among others, discussed undulant fever before the Fourth District Medical Society in Seymour, May 8.——Included among the speakers before the Sixth District Medical Society in Brookville, May 15, was Dr. Eslie Asbury, Cincinnati, on osteomyelitis.——The Ninth District Medical Society was addressed in Attica, May 16, by Drs. Frank Cregor and Robert M. Moore, Indianapolis, on "Drip Treatment of Syphilis" and "Significance of Chest Pain and Its Relation to Heart Disease."——Included among the speakers before the Tenth District Medical Society in Hammond, May 23, will be Drs. Lewis J. Pollock, Chicago, on "Neurological Examination of a Patient" and Morris Fishbein, Chicago, Editor of THE JOURNAL, "American Medicine and the National Government."——Among others, Dr. Samuel M. Feinberg, Chicago, addressed the Eleventh District Medical Society in Huntington, May 15, on "Allergic Diseases of the Summer."

IOWA

Annual Renewal Fees Due Before June 1.—All licenses to practice medicine and surgery in Iowa expire annually on June 30. To renew such a license a licentiate must make a written application to the state department of health before June 1, enclosing the renewal fee of $1. If a license expires by reason of the licentiate's failure to renew it, it can be reinstated without reexamination only on the recommendation of the state department of health and the payment of the overdue fees.

Society News. — Dr. Paul Titus, Pittsburgh, discussed "Recent Advances in Obstetrics" before the Linn County Medical Society, Cedar Rapids, recently. —— Dr. Robert L. Fenton, Centerville, discussed "Modern Treatment of Hemorrhoids and Associated Conditions" before the Lucas County Medical Society recently. —— The Des Moines Academy of Medicine and Polk County Medical Society were addressed in Des Moines recently by Dr. Joseph F. Biehn, North Chicago, Ill., on "Therapeutic Implications of Medical Research." ——Dr. Thomas G. Orr, Kansas City, Mo., addressed the Boone-Story county medical societies in Ames, March 28, on "Intestinal Obstruction." The society was addressed, April 18, by Dr. Robert D. Schrock, Omaha, on "Fractures of the Elbow." —— The Marshall County Medical Society was addressed, April 2, by Dr. Stuart C. Cullen, Iowa City, on "Local and General Anesthesia in Obstetrics and Major Surgery."

MAINE

Society News.—The Kennebec County Medical Association was addressed recently by Dr. George R. Brow, Montreal, Que., on "Cardiac Emergencies and Their Treatment."—— At a meeting of the Portland Medical Club recently Dr. Elton R. Blaisdell discussed "Treatment of Massive Hemorrhage in Gastric and Duodenal Lesions" and Dr. Jack Spencer, "X-Ray Studies of Gastric and Duodenal Lesions."

MICHIGAN

Annual Concert of Glee Club.—The sixth annual concert of the Glee Club of the Wayne County Medical Society was presented at the Detroit Institute of Art, April 29. Marcus Kellerman is director of the club. At the concert the accompanists were Dr. Henry S. Brown on the organ and Dr. Eugene M. Savignac on the piano.

Changes in Health Officers. — Dr. Eldred V. Thiehoff, director of district health department number 7, with headquarters at Gladwin, has been appointed assistant director of the bureau of local health services in the state health department, effective April 1.——Dr. Wallace M. Chapman, Harrodsburg, Ky., has been appointed health officer of district health department number 3, including the counties of Antrim, Charlevoix, Emmet and Otsego, succeeding Dr. Carleton Dean of Lansing.

MINNESOTA

Society News.—Dr. Woodbridge E. Morris, New York, discussed "Birth Control in the Public Health Program" before the Hennepin County Medical Society, May 8, in Minneapolis. —— Dr. John A. Lepak, St. Paul, addressed the Minnesota Academy of Medicine, May 8, on "Eosinophilic Leukemia or Myelogenous Leukemia with Eosinophilic Hyperleukocytosis. Case Report with a Discussion of the Medical Literature."

Continuation Courses. — The Center for Continuation Study at the University of Minnesota is conducting a group of medical and hospital continuation courses, the first of which opened, April 1-6, on venereal disease. Others are:

Obstetrics, April 29-May 1.
Health Problems of College Students, May 2-4.
Electrocardiography, May 13-18.
Diseases of Infancy and Childhood, May 20-25.
Hospital, Medical and Institutional Library Service, May 22-24.
Gynecologic Tumors, June 6-8.

A course in surgical pathology with special attention to tumors will be held June 17-July 26.

NEW JERSEY

Mass Meeting to Discuss Socialized Medicine. — The Bergen County Medical Society will sponsor a public mass meeting for discussion of "Socialized Medicine" at the Teaneck High School, June 7. The speakers will be Drs. Morris Fishbein, Chicago, Editor of THE JOURNAL, and Joseph H. Kler, New Brunswick.

Treasurer for Twenty-Eight Years. — Dr. Robert H. Rogers, Newark, was honored at a meeting of the Essex County Medical Society, Newark, March 14, in recognition of twenty-eight years of service as treasurer of the society. Dr. Rogers received resolutions of appreciation, a watch-charm key of honor and a purse as mementoes of the occasion.

Society News.—Dr. Louis Tuft, Philadelphia, addressed the Atlantic County Medical Society, Atlantic City, April 12, on "Methods of Diagnosis and Principles of Treatment in Allergic Diseases."——Dr. Stanford W. Mulholland, Philadelphia, spoke on "Pyelitis and the Problem of Renal Infections" at a meeting of the Cumberland County Medical Society at Jericho, April 9.——Drs. Fenwick Beekman and Herbert M. Bergamini, New York, addressed the Bergen County Medical Society, Englewood, April 9, on "Osteomyelitis" and "Fractures of the Neck of the Femur" respectively.——Dr. Foster Kennedy, New York, addressed the Hudson County Medical Society, Jersey City, April 2, on "A Critique of Present Trends in Medical Education."——Dr. Frank R. Ober, Boston, addressed the Academy of Medicine of Northern New Jersey, April 18, on "Lame Backs." Dr. Hayes E. Martin, New York, addressed the section on eye, ear, nose and throat, April 8, on "Diagnosis and Curability of Intra-Oral Cancer" and "Cancer of the Eyelid."

NEW YORK

Fifty Years a Practitioner.—Dr. John H. Pratt, Manchester, was honored at a testimonial dinner given by the Ontario County Medical Society in Canandaigua, April 9, in recognition of his fifty years of medical practice and of membership in the society. Dr. Terry M. Townsend, New York, president of the Medical Society of the State of New York, made the principal address. Dr. Pratt graduated from Bellevue Hospital Medical College, New York, in 1890 and entered practice in Manchester the same year with his father, Dr. John Richmond Pratt, who completed fifty years of practice in 1904. Both Dr. Pratt and his father served as president of the county medical society. Dr. Pratt is the grandson of Dr. Franklin B. Hahn, who practiced in Canandaigua from 1820 to 1850 and was secretary of the society for several years. According to the present secretary of the society, Dr. Pratt is the ninth physician to have completed fifty consecutive years as a member.

Society News. — Dr. James B. Collip, Montreal, Que., Canada, addressed the Medical Society of the County of Westchester, White Plains, April 16, on "Recent Work in Pituitary Physiology."——Dr. Charles A. Weymuller, Brooklyn, addressed the Onondaga County Medical Society, Syracuse, April 2, on "Recent Advances in Pediatrics." —— Dr. Alexander S. MacMillan, Boston, addressed a joint meeting of the Syracuse Academy of Medicine and Syracuse Eye, Ear, Nose and Throat Club, April 16, on "X-Ray Interpretation of the Respiratory Tract, the Mastoids and the Skull."—— Dr. A. Benson Cannon, New York, addressed the Dutchess County Medical Society in Poughkeepsie, April 10, on "Present Day Viewpoint on Skin Diseases" and Dr. Paul W. Harrison, Muscat, Arabia, "Medical and Surgical Practice in Arabia." ——Dr. Nicholson J. Eastman, Baltimore, discussed "Obstetric Hemorrhage" before the Rochester Academy of Medicine, April 3.

New York City

Eighth Harvey Lecture.—Rudolph J. Anderson, Ph.D., professor of chemistry, Yale University, New Haven, Conn., delivered the eighth Harvey Society Lecture of the season at the New York Academy of Medicine, May 16. His subject was "The Chemical Composition of the Lipoids of the Tubercle Bacillus."

Mickle Award to Columbia Anatomist.—Philip E. Smith, Ph.D., professor of anatomy at Columbia University College of Physicians and Surgeons, recently received the Charles Mickle Fellowship of the University of Toronto in recognition of his work on the pituitary gland, according to the New York *Times*. This fellowship is the annual income from an endowment fund of $25,000 and is awarded to the scientist who, in the opinion of the council of the university, has done most during the preceding ten years to advance sound knowledge of a practical kind in medical art or science. Dr. Smith has taught anatomy at Cornell University, the University of California and Stanford University and has been professor at Columbia since 1927.

Courses at Post-Graduate School.—The New York Post-Graduate Medical School announces several courses planned to coordinate with the annual session of the American Medical Association in New York, June 10-14. An intensive course in "Clinical Interpretations of Laboratory Data" will be given under the direction of Dr. Maurice Bruger, June 3-7. A course on "Diseases of the Liver and Biliary Tract" will be presented June 3-8 under the direction of Drs. Rupert Franklin Carter, Carl H. Greene and John Russell Twiss. Following the convention a ten day symposium in medicine will be offered under Dr. Walter G. Lough. In addition the school announces a seminar in pediatrics for the month of July under Dr. Adolph G. G. DeSanctis. Information may be obtained from the Director, 309 East Twentieth Street.

NORTH CAROLINA

District Meetings on Cancer. — The Eighth District Medical Society held its spring meeting in Greensboro, April 11, with Dr. John Shelton Horsley, Richmond, Va., as the guest speaker on "Principles of Treatment and Handling of Cancer Patients." A symposium on early signs and symptoms of cancer was presented by Drs. Booker E. Rhudy and Russell O. Lyday, Greensboro; Arthur deT. Valk, Charles O. DeLaney and Robert A. Moore, Winston-Salem; Harry L. Brockmann, High Point; Moir S. Martin, Mount Airy, and Wayne J. Benton, Greensboro. —— At a meeting of the Ninth District Medical Society in Statesville, April 4, Dr. Milton Friedman, New York, was the guest speaker on "Benign and Malignant Tumors of the Breast." Other speakers were Drs. Thomas V. Goode, Statesville, on "Diagnosis of Cancer"; Angus Hinson, Statesville, "Diagnosis and Treatment of Malignancy of the Cervix Uteri"; Joseph Rush Shull, Charlotte, "Irradiation of Metastatic Malignancy," and Coy C. Carpenter, Wake Forest, "Responsibility of the Clinician in the Pathologic Diagnosis of Tumors."

PENNSYLVANIA

Personal.—Dr. Ronald B. McIntosh has resigned as head of the Selinsgrove State Colony for Epileptics, it is reported. —— Dr. Verne G. Burden, Philadelphia, has been appointed superintendent of the Eastern State Penitentiary to succeed Dr. Basil R. Beltran, resigned.——Dr. Amos W. Gottschall has resigned as superintendent of the Chester County Hospital for the Insane, Embreeville, and has been succeeded by Dr. John M. Mras, Philadelphia, it is reported.

Society News. — Dr. Mark M. Bracken, Pittsburgh, addressed the Blair County Medical Society, Altoona, March 19, on "Blood Requirements in Transfusion."——Dr. Temple S. Fay, Philadelphia, discussed "Human Refrigeration" before the Delaware County Medical Society, Chester, April 11.—— Dr. William M. Skipp, Youngstown, Ohio, addressed the Mercer County Medical Society, Grove City, April 10, on "Thyroid Diseases." —— Dr. William Bates, Philadelphia, addressed the Dauphin County Medical Society, Harrisburg,

April 2, on "Parietal versus Visceral Pain and Tenderness." ——Dr. James H. Rankin Jr., Woodville, addressed the Washington County Medical Society, Washington, April 10, on "Metrazol Treatment of Insanity, with Special Reference to Prevention of Fracture Complications." —— Drs. Charles W. Mayo, Rochester, Minn., and Ralph Lynch, Pittsburgh, addressed the Cambria County Medical Society, Johnstown, April 11, on "Perineal Resection of Malignant Lesions of the Lower Sigmoid, Rectosigmoid and Rectum" and "Prothrombin Deficiency—Its Clinical Importance and Management" respectively. The guests also conducted clinics in the afternoon at the Conemaugh Valley Memorial Hospital.——Dr. Joseph T. Beardwood Jr., Philadelphia, addressed the Lebanon County Medical Society, Lebanon, April 9, on "New Aspects of Diabetes and Its Treatment."

Philadelphia

Courses for Graduate Physicians. — The Pennsylvania Hospital announces its 1940 postgraduate courses in internal medicine, June 3-21. A course in cardiology will be given June 3-7 and one on diseases of metabolism June 17-21. Other subjects will be gastro-enterology, hematology, diseases of the lungs and diseases of the kidneys. Information may be obtained from the Registrar of Summer Course, Pennsylvania Hospital, Eighth and Spruce streets, Philadelphia.

Dr. Bronk Goes to Cornell.—Detlev W. Bronk, Ph.D., Eldridge Reeves Johnson professor of biophysics and director of the Johnson Foundation for Medical Physics at the University of Pennsylvania School of Medicine, has been appointed head of a new department of physiology and biophysics at Cornell University Medical College, New York. Dr. Bronk took his doctor's degree at the University of Michigan in 1926 and served on the faculty at Michigan and Swarthmore College before coming to Pennsylvania in 1929. Recently he has also been vice dean for neurology and professor of neurology in the graduate school of medicine and director of the Institute of Neurology of the University of Pennsylvania. According to the New York *Times*, five other members of the staff at the University of Pennsylvania were also appointed to the new department at Cornell: Dr. H. Keffer Hartline, Arthur J. Rawson, M.E., John P. Hervey, M.S., Martin G. Larrabee, Ph.D., and Frank Brink Jr., M.S.

Pittsburgh

Mellon Lecture.—Philip A. Shaffer, Sc.D., professor of biologic chemistry and dean, Washington University School of Medicine, St. Louis, delivered the annual Mellon Lecture on May 9 at Mellon Institute. Dr. Shaffer's subject was "The Mode of Action of Sulfanilamide—Another Enigma of Chemotherapy." This lecture is sponsored by the Society for Biological Research at the University of Pittsburgh School of Medicine.

TEXAS

District Meeting.—The Eleventh District Medical Association met in Tyler, April 4, with the following program:

Dr. Meyer Bodansky, Galveston, The Role of Vitamins in Clinical Medicine.
Dr. Donovan C. Browne, New Orleans, Management of Peptic Ulcer Hemorrhage.
Dr. Willis C. Campbell, Memphis, Tenn., Treatment of Compound Fractures.
Dr. Thomas Leon Howard, Denver, Hematuria.
Dr. Albert O. Singleton, Galveston, Diaphragmatic Hernia.

Dr. Leopold H. Reeves, Fort Worth, president of the State Medical Association of Texas, spoke at a luncheon on "Organized Medicine."

WASHINGTON

Prize Awarded to Dr. Brien T. King.—The American Association for the Study of Goiter at its annual meeting in Rochester, Minn., April 15-17, awarded the Van Meter Prize of $300 to Dr. Brien T. King, Seattle, for his essay on "A New and Function-Restoring Operation for Bilateral Abductor Cord Paralysis." Honorable mention was given to Dr. Irving M. Ariel, William Bale, Ph.D., Vincent F. Downing, B.S., Walter Mann, B.S., Harold C. Hodge, Ph.D., Dr. Stafford L. Warren and Stanley Van Voorhis, Ph.D., Rochester, N. Y. for an essay on "Preliminary Study of Variations in the Distribution of Radioactive Iodine in Normal Rabbits" and to Dr. Doran J. Stephens, Rochester, N. Y., for a paper on "Effects of the Thyrotropic Principle of the Anterior Pituitary on the Thyroid Gland of the Undernourished Guinea Pig."

GENERAL

Conference of Negro Tuberculosis Workers.—The second annual conference of Negro tuberculosis workers will be held at Howard University School of Medicine, Washington, D. C., May 27-28, under the auspices of the Tuberculosis Association of the District of Columbia and the National Tuberculosis Association.

Fellowships in Cancer. — The Finney-Howell Research Foundation, Baltimore, has announced Jan. 1, 1941, as the closing date for filing applications for 1941 awards in cancer research. Announcement was also made of a grant of $2,000 to Dr. George O. Gey to carry on his work in cancer at Johns Hopkins University School of Medicine. In addition, seven fellowships for investigation into the cause or causes and the treatment of cancer were renewed by the foundation at its annual meeting in March and six new fellowships were awarded.

Summer Classes for Sight-Saving Teachers. — The National Society for the Prevention of Blindness announces the following summer courses for the preparation of teachers and supervisors of sight-saving classes:

Oregon State System of Higher Education, Portland, Ore., elementary course, June 17 to July 26, under Miss Olive S. Peck, Cleveland.
Wayne University, Detroit, elementary course, June 24 to August 2 or July 1 to August 9, under Miss Margaret M. Soares, Detroit.
State Teachers College, Buffalo, N. Y., elementary course, July 1 to August 9, under Miss Matie M. Carter, Albany, N. Y.
University of Minnesota, Minneapolis, advanced course, June 17 to July 26, under Mrs. Winifred Hathaway, New York.

Annual Dinner of Obstetric Board.—The annual dinner of the American Board of Obstetrics and Gynecology will be held at the Hotel McAlpin, New York, Wednesday evening, June 12. Diplomates certified at the preceding days' examination will be introduced and there will be several speakers. All diplomates of the board and others interested in the work of the board are cordially invited. Tickets at $3.50 each may be obtained from Dr. Joseph L. Baer, chairman, 104 South Michigan Avenue, Chicago, or at the registration desk during the examinations. For further information address Dr. Paul Titus, secretary of the board, 1015 Highland Building, Pittsburgh.

American Otological Society.—The seventy-third annual meeting of the American Otological Society will be held at the Westchester Country Club, Rye, N. Y., May 30-31, under the presidency of Dr. Horace Newhart, Minneapolis, whose subject will be "Conservation of Hearing." The program includes a symposium on the recognition, treatment and prevention of hearing impairment in children and panel discussions on "Infectious Lateral Sinus Thrombophlebitis" and "Information Please: Regarding Hearing Aids and Audiometers." Other speakers will include:

Dr. Hallowell Davis, Boston, The Clarification of Certain Phases of the Physiology of Hearing.
Dr. Champ Lyons, Boston, The Causes of Sulfanilamide Failures.
Willis C. Beasley, Ph.D., Bethesda, Md., The General Problem of Deafness in the Population.
F. H. Shepard Jr., Merchantville, N. J., A New Amplifier Having Characteristics Similar to Those of the Human Ear, and Its Application to the Problem of Deafness.

Alumni Reunions.—The class of 1930 of Columbia University College of Physicians and Surgeons will hold its tenth reunion during the annual session of the American Medical Association in New York. The 1930 alumni will occupy a table at the dinner of the Alumni Association of the College of Physicians and Surgeons, June 12, at the Columbia University Club. Dr. Charles A. Perera, 70 East Sixty-Sixth Street, New York, is secretary of the class.——Phi Lambda Kappa Fraternity will hold a luncheon at the Longchamps Restaurant, New York, June 12. Reservations may be obtained at the Phi Lambda Kappa booth at the American Medical Association meeting or by addressing Dr. Herman Wechsler, 214 Echo Place, Bronx, N. Y.——The alumni of Creighton University Medical School, Omaha, will hold a banquet during the annual session of the American Medical Association in New York, June 12, in the North Ballroom, Hotel New Yorker. Reservations may be made through Dr. Carl R. Palmer, Hotel New Yorker, New York. The banquet will be informal, $3.50 per plate.

American Dermatological Association.—The sixty-third annual meeting of the American Dermatological Association will be held at the Broadmoor Hotel, Colorado Springs, May 30-June 1, under the presidency of Dr. Frank Crozer Knowles, Philadelphia. Among the speakers announced are:

Dr. Frederick R. Schmidt, Chicago, Iodine in the Treatment of Diseases of the Skin: The Influence of Climate and the Weather.
Dr. Francis W. Lynch, St. Paul, The Histopathology of Acne.

Dr. Charles C. Dennie, Kansas City, Mo., Massive Destruction of the Face.
Dr. A. Benson Cannon, New York, A Clinical and Laboratory Study of Epidermolysis Bullosa.
Drs. Francis E. Senear and Marcus R. Caro, Chicago, Lichen Striatus.
Dr. Louis A. Brunsting and Charles Sheard, Ph.D., Rochester, Minn., A Study of Dark Adaptation in Cases of Pityriasis Rubra Pilaris.
Dr. Carroll S. Wright, Philadelphia, Vitamin D Therapy in Dermatology.
Dr. William H. Goeckerman, Los Angeles, Some Injurious Effects of Arsenic.
Dr. Howard J. Parkhurst, Toledo, Ohio, Toilet Soaps, Soap Substitutes and Hard Water: A Study of Various Combinations by Patch Tests.

Association for Research in Ophthalmology. — The eleventh scientific meeting of the Association for Research in Ophthalmology will be held in New York at the Biltmore Hotel, June 11. Papers to be presented will be:

Drs. Theodore L. Terry, Boston, and Julian F. Chisholm, Savannah, Ga., Effect of Pressure on Conical Cornea.
Dr. Irving Puntenney, Chicago, Effect of Certain Physical and Chemical Stimuli on the Caliber of the Retinal Vessels in Man.
Drs. Erich Sachs and Parker Heath, Detroit, Pharmacologic Experiments on Isolated Segments of Mammalian Iris.
Dr. Loren P. Guy, New York, Passage of Horse Serum from the Blood Stream into the Aqueous Humor of Normal and Immunized Animals.
Dr. Phillips Thygeson, New York, Cultivation of Conjunctivitis and Keratitis Producing Agents on the Chorio-Allantoic Membrane of the Chick Embryo.
Dr. Kenneth C. Swan and William Hart, M.A., Iowa City, A Comparative Study of the Effects of Mecholyl, Doryl, Eserine, Pilocarpine, Atropine and Epinephrine on the Blood-Aqueous Barrier.
Dr. Karl Meyer and Eleanor Chaffee, New York, The Mucopolysaccharide Acid of the Cornea and Its Enzymatic Hydrolysis.
Drs. Lincoln F. Steffens and Hugo L. Bair and Charles Sheard, Ph.D., Rochester, Minn., Dark Adaptation of Normal Adults on Diets Deficient in Vitamin A.

American Heart Association. — The sixteenth scientific sessions of the American Heart Association will be held at the Hotel Roosevelt, New York, June 7-8, under the presidency of Dr. William D. Stroud, Philadelphia. The speakers will include:

Dr. John M. Askey, Los Angeles, The Syndrome of Painful Disability of the Shoulder and Hand Complicating Coronary Thrombosis.
Drs. Helen B. Taussig and Marcellus Goldenberg, Baltimore, Studies in Cardiac Enlargement in Children with Rheumatic Heart Disease.
Dr. Arthur L. Smith, Lincoln, Neb., Fetal Heart Sounds in Fifty-Two Cases.
Drs. Edgar V. Allen and George E. Brown, Rochester, Minn., Simplified Method of Producing Continuously an Increased Blood Flow to the Extremities: Clinical and Physiologic Studies.
Drs. Gilbert H. Marquardt and Alexander Sanders, Chicago, Correlation of Peripheral Vasospasm and Angina Pectoris Attacks.
Drs. Hugh Montgomery, Meyer Naide and Norman E. Freeman, Philadelphia, Diagnostic Procedures in Peripheral Arterial Disease.

Dr. Louis Hamman, Baltimore, will deliver the Lewis A. Conner Lecture, Friday, on "Coronary Embolism" and Dr. Henry C. Bazett, Philadelphia, the George Brown Memorial Lecture, Saturday, on "Blood Volume and Cardiovascular Adjustments."

American Proctologic Society. — The forty-first annual meeting of the American Proctologic Society will be held in Richmond, Va., June 9-11, with headquarters at the Jefferson Hotel and under the presidency of Dr. Martin S. Kleckner, Allentown, Pa. Dr. Alois B. Graham, Indianapolis, will deliver the biennial Joseph M. Matthews Oration, on "An Appraisal of the American Proctologic Society." The program will include a symposium on anal pruritus by Drs. Theodore F. Reuther, Chicago, on "The Nerves of the Anorectal Region," and Malcolm R. Hill, Los Angeles, "The Etiologic Relationship Between Dermatophytosis and Pruritus Ani." In addition, the following papers will be presented, among others:

Dr. Thomas T. Mackie, New York, The Role of Avitaminosis in Rectal Bleeding.
Dr. Curtis C. Mechling, Pittsburgh, Metastasis from Rectal and Colonic Tumors.
Dr. Walter A. Fansler, Minneapolis, Diverticulosis and Diverticulitis.
Drs. Harry E. Bacon and Hesser C. C. Lindig, Philadelphia, Spinal Anesthesia.
Dr. Edward G. Martin, Detroit, The Technic of Permanent Colostomy.
Dr. Douglass Palmer, New York, Present Day Diagnosis of Diseases of the Colon.
Dr. Kenneth E. Smiley, Los Angeles, Repair of the Sphincter Ani with Alloy Steel Sutures.

Registration Under Harrison Narcotic Act and the Marihuana Tax Act.—On or before July 1, every physician registered under the Harrison Narcotic Act or under the Marihuana Tax Act, or under both, must reregister with the collector of internal revenue of each district in which he maintains an office or a place for the treatment of patients. Failure to reregister within the time allowed by law adds a penalty of 25 per cent to the annual tax payable at the time of registration and in addition makes the physician in default liable to a fine not exceeding $2,000, or to imprisonment for not exceeding five years, or to both. In recent years the Commissioner of Internal Revenue has given some negligent or recalcitrant physicians the choice between paying substantial sums by way of compromise in lieu of the penalties for their offenses or, as an alternative, accepting criminal prosecution with resultant publicity and liability to fines and possible imprisonment. This was an act of grace on the part of the commissioner; he might have instituted criminal prosecutions without allowing the offending physicians any choice in the matter. If the course that the commissioner has adopted does not produce the desired promptness in registration, he will have no recourse other than criminal prosecution to attain that result.

Meeting of Chest Physicians. — The American College of Chest Physicians will hold its sixth annual meeting at the Biltmore Hotel, New York, June 8-10, under the presidency of Dr. Ralph C. Matson, Portland, Ore. Among papers to be presented are the following:

Dr. Richard H. Overholt, Brookline, Mass., Extrapleural Pneumothorax: A Report of Experiences and Present Day Indications.
Dr. Herbert R. Edwards, New York, Case Finding: A Fundamental in Tuberculosis Control.
Dr. Andrew L. Banyai, Wauwatosa, Wis., Newer Aspects of the Pneumoperitoneum Treatment of Pulmonary Tuberculosis.
Dr. Louis H. Clerf, Philadelphia, Bronchoscopy in Bronchial Obstruction.
Dr. William F. Rienhoff Jr., Baltimore, Surgical Management of Carcinoma of the Lung.
Drs. Harold Brunn and Sidney J. Shipman, San Francisco, Certain Aspects of Intrapulmonary Cavitation.

There will be "Information Please" luncheons on Saturday and Sunday with groups of experts to answer questions. Monday there will be clinics at Lenox, Kings County, Montefiore, Sea View, Bellevue and Kingston Avenue hospitals and the group will attend a symposium on tuberculosis to be presented in the Section on Practice of Medicine of the American Medical Association.

National Gastroenterological Association. — The fifth annual convention of the National Gastroenterological Association will be held at the Hotel Roosevelt, New York, June 4-6, under the presidency of Dr. Anthony Bassler, New York. Invited speakers on the program include:

Dr. William Wayne Babcock, Philadelphia, Diverticulitis.
Dr. Chester S. Keefer, Boston, The Fatty Liver: Its Clinical Features and Clinical Course.
Dr. Robert M. Zollinger, Boston, Surgical Treatment of Gallbladder Disease.
Dr. Richard B. Cattell, Boston, Indications for and the Results of Complete Colectomy in Chronic Ulcerative Colitis.
Drs. Charles A. Doan, Philip T. Knies and Clark P. Pritchett, Columbus, Ohio, Gastroscopic Studies of Multiple Erosions of the Human Gastric Mucosa with Prompt Response to Histaminase.
Dr. Willard D. Mayer, Detroit, Further Observations on the Use of Food in the Treatment of Bleeding Peptic Ulcer (Meulengracht Diet).
Dr. Boris P. Babkin, Montreal, Canada, The Influence of the Parathyroid Glands on the Secretory Processes of the Stomach.
Dr. James D. Adamson, Winnipeg, Man., John Abercrombie and His Work on Gastric Ulcers.
Dr. James Harvey Black, Dallas, Texas, Gastrointestinal Allergy.
Dr. Tate Miller, Dallas, Indications and Contraindications of Medical Treatment of Gallbladder Diseases and Duodenal Ulcer.
Dr. Harry P. Smith, Iowa City, Vitamin K: Its Use in Patients with Obstructive Jaundice or with Biliary Fistula.

Tuberculosis Organizations Meet in Cleveland. — The annual meetings of the National Tuberculosis Association, the American Trudeau Society and the National Conference of Tuberculosis Secretaries will be held in Cleveland, June 3-6, with headquarters at the Hotel Statler. The medical and administrative sections will hold separate sessions the first two days and a joint session the third day; the tuberculosis association and the Trudeau Society will meet on the fourth day jointly with the American Association for Thoracic Surgery, which meets June 6-8. Among the medical papers listed on the program are:

Drs. Richard M. McKean, George C. Thosteson and Nathan Brooks, Detroit, Treatment of Tuberculosis and Diabetes, A Ten Year Experience.
Drs. Lynne E. Baker, James N. Christiansen and McKinnie L. Phelps, Cincinnati, Tuberculous Empyema.
Dr. Maxim Pollak, Peoria, Ill., Tuberculosis in Mental Institutions.
Dr. Harry J. Corper, Denver, Chemotherapy in Tuberculosis.
Dr. William H. Weidman, Norwich, Conn., The Application of Laminagraphy in Chest Conditions.
Dr. Fred H. C. Heise, Trudeau, N. Y., Constitutional Factors and Diet in Tuberculosis.
Drs. Andre Cournand and Dickinson W. Richards Jr., New York, and Herbert C. Maier, Ann Arbor, Mich., Functional and Physiologic Disturbances Following Severe Thoracic Deformities.

Meeting of Clinical Pathologists.—The American Society of Clinical Pathologists will hold its nineteenth annual meeting and seventh seminar at the Hotel Biltmore, New York, June 7-9, under the presidency of Dr. Leonard W. Larson, Bismarck, N. D., whose subject will be "The Clinical Pathologist." Among the speakers will be:

Drs. James B. McNaught, Rodney R. Beard, and Jack D. Myers, San Francisco, Diagnosis of Trichinosis by Skin and Precipitin Tests.
Drs. Max M. Strumia, Joseph A. Wagner, Bryn Mawr, Pa., and James Frederick Monaghan, Philadelphia, Use of Citrated Plasma, Fresh and Preserved and the Institution of Plasma Banks.
Drs. Nathan Rosenthal, Frank A. Bassen and Peter Vogel, New York, Importance of Sternal Puncture as a Diagnostic Aid in Hematologic Conditions.

Dr. Maxwell M. Wintrobe, Baltimore, Summary and Evaluation of Sedimentation Tests.
Dr. Walter W. Jetter, Taunton, Mass., and Dr. Merrill Moore, Boston, and Glenn C. Forrester, Ph.D., Niagara Falls, N. Y., A New Method for the Determination of Breath Alcohol Using Magnesium Perchlorate.

At the tumor seminar, Sunday, Dr. James Ewing, New York, will speak on "Problem Tumors of the Breast." E. P. Coffey, chief, technical laboratory, Federal Bureau of Investigation, U. S. Department of Justice, Washington, D. C., will address the banquet session on "What the Medical Profession Contributes to Crime Detection."

Ear, Nose and Throat Meeting.—The forty-sixth annual meeting of the American Laryngological, Rhinological and Otological Society, Inc., will be held at the Hotel Waldorf-Astoria, New York, June 6-8. Among the speakers will be:

Dr. Austin A. Hayden, Chicago, Hearing Aids—Indications for Their Use.
Dr. Edmund P. Fowler, New York, Head Noises—Significance, Measurement, and Importance in Diagnosis and Treatment.
Dr. Frederick T. Hill, Waterville, Me., A Study of Mortality Records Over a Ten Year Period.
Dr. Hermon Marshall Taylor, Jacksonville, Absorption of Quinine into the Cerebrospinal Fluid of the Fetus in Utero.
Dr. Louis H. Clerf, Philadelphia, Cancer of the Larynx.
Dr. Hayes E. Martin, New York, The Selection of the Method of Treatment in Laryngeal Cancer.
Dr. Frederic W. Bancroft, New York, The Use of Anticoagulants in Thrombosis and Embolism.
Dr. Martin R. Steinberg, Philadelphia, The Role of Oxalic Acid and Related Di-Carboxylic Acids in the Treatment and Control of Hemorrhage (co-authors: Drs. Hyman I. Segal and Herman M. Parris, both of Philadelphia).
Dr. Alfred J. Cone, St. Louis, The Use of Salt Pork in Hemorrhages.
Dr. French K. Hansel, St. Louis, The Treatment of Allergy of the Nose and Paranasal Sinus by Hyposensitization with Dust Extracts.
Dr. Warren T. Vaughan, Richmond, Va., Special Allergic Diagnostic Methods Appropriate for the Rhinologist.
Dr. Elbyrne G. Gill, Roanoke, Va., The Management of Thyroglossal Cyst, with Report of Ten Cases.
Dr. Rea E. Ashley, San Francisco, Surgical and Non-Surgical Treatment of the Chronically Discharging Middle Ear.
Dr. Henry L. Williams, Rochester, Minn., Roentgen Therapy for Acute Sinusitis.

Meetings on Industrial Medicine.—The twenty-fifth annual meeting of the American Association of Industrial Physicians and Surgeons will be held in New York at the Hotel Pennsylvania, June 6-7, under the presidency of Dr. McIver Woody, New York. Among the speakers announced are:

Dr. John J. Moorhead, New York, Care and Handling of Traumatic Injuries.
Dr. Byron P. Stookey, New York, Problems in Diagnosis and Management of the Nucleus Pulposus.
Dr. Marion B. Sulzberger, New York, Occupational Dermatitis.
Dr. Irving S. Wright, New York, Trauma and the Peripheral Vascular System.

Preceding the meeting of the physicians and surgeons will be the first annual meeting of the American Industrial Hygiene Association, June 4-5, under the presidency of Mr. William P. Yant, Pittsburgh. Among addresses to be delivered will be:

Donald E. Cummings, B.S., director, division of industrial hygiene, University of Colorado School of Medicine, Denver, Industrial Hygiene in Steel Plant Practice.
Hervey B. Elkins, Ph.D., chief chemist, division of occupational hygiene, Massachusetts Department of Labor and Industry, Boston, Exposure to Mercury in the Manufacture of Felt Hats.
H. W. Ruf, industrial hygiene unit, Wisconsin State Board of Health, Madison, Wis., and Dr. Elston L. Belknap, Milwaukee, Studies of the Lead Hazard in Printing.
William R. Bradley, bureau of industrial hygiene, city board of health, Detroit, Animal Studies on the Toxicity of Antimony.

Meeting of Psychiatrists.—The ninety-sixth annual meeting of the American Psychiatric Association will be held at the Netherland Plaza Hotel, Cincinnati, May 20-24, under the presidency of Dr. William C. Sandy, Harrisburg, Pa. Among the speakers will be:

Dr. Hiram Houston Merritt, Boston, A Report on New Drugs for the Treatment of Epilepsy and a Further Report on the Results of the Use of Dilantin.
Dr. Burtrum C. Schiele, Minneapolis, A Clinical Study of Sleep Disturbances.
Dr. William Y. Baker, Seattle, Carbohydrate Metabolism in Relation to Anxiety States.
Drs. Hugh T. Carmichael, Allan T. Kenyon and William J. Noonan, Chicago, The Effects of Testosterone Propionate in Impotence.
Dr. András Angyal and Nathan Blackman, Worcester, Mass., Vestibular Reactivity in Schizophrenic and Normal Individuals.

There will be symposiums and round table discussions. At the annual dinner, Wednesday, Major Norman A. Imrie, associate editor, Columbus *Dispatch*, Columbus, will give an address entitled "Victory by Surprise." A public meeting will be held in the Taft Auditorium, Monday evening, in cooperation with the Cincinnati Academy of Medicine, Cincinnati Medical Hygiene Council and the Public Health Federation. Dr. Emerson A. North, professor of psychiatry, University of Cincinnati College of Medicine, will open the meeting with Dr. Rock Sleyster, Wauwatosa, Wis., President, American Medical Association, the presiding officer. The speakers will be Drs. Edward A. Strecker, Philadelphia, on "Alcoholism—A Personal and Social Problem"; Helen Flanders Dunbar, New York, "Medicine Yesterday and Today," and Winfred Overholser, Washington, D. C., "Facts and Fiction About State Mental Hospitals." The American Psychopathological Association will meet at the Hotel Netherland Plaza, May 18-19, and the American Psychoanalytic Association, May 19-22.

American Rheumatism Association.—The annual meeting of the American Rheumatism Association will be held at the Hotel Waldorf-Astoria, New York, June 10, under the presidency of Dr. Philip S. Hench, Rochester, Minn. Included on the program will be:

Dr. William T. Green, Boston, Mono-Articular and Pauci-Articular Arthritis in Children.
Dr. Robert M. Stecher, Cleveland, Heberden's Nodes: Heredity in Hypertrophic Arthritis of the Finger Joints.
Dr. Otto Steinbrocker, New York, Local and Regional Analgesic Injections in the Treatment of Intractable, Nonsurgical Shoulder Conditions.
Dr. May G. Wilson, New York, Dr. Ralph E. Wheeler, Bethesda, Md., and Morton D. Schweitzer, Ph.D., New York, The Familial Epidemiology of Rheumatic Fever.
Drs. Daniel Murray Angevine, Sidney Rothbard and Russell L. Cecil, New York, Cultural Studies on Rheumatoid Arthritis and Rheumatic Fever.
Drs. Otto Rosenthal, Philadelphia, Morris A. Bowie, Bryn Mawr, Pa., and George W. Wagoner, Philadelphia, Metabolism of Cartilage (Bovine) with Particular Reference to the Effects of Aging.
Drs. Ward Darley Jr. and Robert W. Gordon, Denver, Latent Brucellosis: Its Importance in Association with Joint, Muscle and Nerve Pain.
Dr. Ralph K. Ghormley, Rochester, Minn., A Discussion of the End Results of Synovectomies of the Knee Joint.
Drs. Charley J. Smyth, Richard H. Freyberg and Willis S. Peck, Ann Arbor, Mich., Experiences with Roentgen Therapy in Various Rheumatic Conditions.

Dr. Hench will deliver his presidential address on "Acute Multiple Recurring Arthritis and Periarthritis: Forty Cases of a New Articular Disease," and E. P. Coffey, chief, technical laboratory, Federal Bureau of Investigation, U. S. Department of Justice, will address the annual dinner on "What the Medical Profession Contributes to Crime Detection."

CANADA

Typhoid Near Winnipeg.—Sixty-four cases of typhoid with four deaths are reported to have occurred in the city of St. Boniface and the municipality of Ste. Anne, near Winnipeg, just previous to April 9, the *Canadian Public Health Journal* reported. The outbreak was attributed to infected food.

Personal.—Dr. John C. Mackenzie, general superintendent of the Montreal General Hospital, has been appointed officer in charge of all hospital administration to the Canadian forces in England, according to the *Canadian Medical Association Journal*.——The Honorable Henri Groulx, Montreal, a pharmacist and a member of the provincial legislature, has been appointed provincial secretary and minister of health for Quebec.

CORRECTIONS

The Late Dr. J. P. Widney.—In THE JOURNAL, April 27, p. 1669, column two, it was said that Dr. J. P. Widney is still living in Los Angeles in his ninety-seventh year. Dr. Widney died July 4, 1938, aged 96.

Dr. Himwich Is a Doctor of Medicine.—In an announcement of the program of the Association on Mental Deficiency in THE JOURNAL, page 1942, the name of Dr. Harold E. Himwich, Albany, N. Y., appeared with the Ph.D. degree. Dr. Himwich is a doctor of medicine, having graduated from Cornell University Medical College, New York, in 1919.

The Therapy of Dropsy.—In the special article by Dr. H. M. Marvin on "The Therapy of Dropsy" in THE JOURNAL, March 2, page 759, first column, the sentence beginning in line 16, should read: These are organic mercurial compounds containing respectively 33 to 34.5 per cent and 39.6 per cent of mercury and are effective when administered by intravenous or intramuscular injection or in the form of rectal suppositories. In the second column on the same page, the sentence beginning in line 40 should read as follows: The advantages of combining the two have been so apparent in recent years that many mercurials now marketed in Europe have been modified by the addition of theophylline. Several years ago salyrgan was thus modified and is available under the name salyrgan-theophylline; its content of theophylline is 5 per cent, which is slightly more than the 3.5 per cent found in mercupurin. (The latter is mercurin combined with theophylline.)

Foreign Letters

LONDON

(From Our Regular Correspondent)

April 13, 1940.

Improved Health of the Nation

The population of England and Wales in the middle of 1938 is estimated in the registrar general's statistical review for the year as 41,215,000. The population at the 1931 census was 39,952,377. The births registered during 1938 numbered 621,204. The birth rate was 15.1 per thousand persons living, which was 0.2 above that for 1937, 0.3 above that for 1936 and 0.7 above that for 1933. The last, 14.4, was the lowest ever recorded. The mortality of infants under 1 year was 53 per thousand live births, which was 4 per thousand below the lowest rate on record. Record low rates were also reached for a number of infectious diseases. The mortality from infectious and parasitic diseases in general dropped to 1.01 per thousand, a decrease of 0.16 compared with the previous low record of 1936. Maternal mortality, excluding deaths from abortion, declined for the fourth year in succession to a new low level of 2.62 per thousand births. The death rate from whooping cough per million children under the age of 15 years was 126, while the previous lowest level was 170.

The general death rate was 11.6 per thousand of population and 0.8 below that for 1937. The only year with a lower rate was 1930, when the figure was 11.4. After allowing for the increasing proportion of old people in the population, the corrected or standardized rate was only 8.5, an improvement on the record rate of 1935 by 0.5. But the cancer rate, also standardized to allow for the increasing age of the population, rose slightly, to 1,005 per million from 1,002 in 1937.

Light Armor in Modern Warfare

Mr. Kenneth Walker, a genito-urinary surgeon experienced in the treatment of wounds in front line conditions in the last great war, advocates in the *British Medical Journal* the use of light armor. During the last two years of the war he was occupied touring the third army front, studying such questions as the early treatment of wounds, the combating of surgical shock, the methods of transporting the wounded to the casualty clearing stations and the possibility of transfusion in the regimental aid post. He noted the large number of men who died in the trenches as the result of being hit in the front of the chest by tiny fragments of grenades or shell that ripped open some large vessel with rapidly fatal effect. The most fatal area corresponded to that part of the chest covered by the box respirator when carried in the alert position. Remembering how many men had been saved by the steel helmet, he sent to headquarters a memorandum suggesting that a pocket might be made in the box respirator into which could be slipped a steel plate. By curving the plate to the chest and adding a suitable fastening, it would be possible to attach the plate, when not in use, to a wooden handle, so as to serve as an entrenching tool. The memorandum came to rest in a pigeon hole of the Ministry of Munitions, where it would have remained had not a friend, the late Arthur Asquith, been made controller of trench warfare supplies. He showed it to his chief, Winston Churchill. The result was that Walker was recalled to work at the ministry as expert in light armor. But, as it had taken two years' agitation to introduce the steel helmet and the war was nearly over, he declined the appointment.

The same question now arises. Having accepted the value of protecting the head from projectiles of low penetrating power, Walker asks, Is it not advisable to extend the principle to other vulnerable areas? Of course no armor that a man can support will render him immune to missiles traveling with the momentum of a bullet, but the records show that 60 per cent of the wounded were put out of action by projectiles other than bullets. Sauerbach found that 37 per cent of those found dead on the battle field had chest wounds, while at a British casualty clearing station the percentage was only 3. Thus the vast majority of chest wounds prove fatal from hemorrhage in the trenches.

Salmonella Infections

At the Royal Society of Medicine Sir William Savage opened a discussion on salmonella infections, of which he mentioned four features: (1) The organisms were all true parasites; (2) they never occurred outside the body as saprophytes; (3) they were not natural inhabitants of any animal intestine; (4) when found in animals they represented an old infection and were examples of the carrier state. A large number of types were isolated, certainly over forty, which were not convertible into one another and serologically were distinct. Their pathologic manifestations fell into three groups—continued fever, gastrointestinal irritant action and general infection of the septicemic type. They were widespread as a cause of disease in man, mammals and birds. Prevention depended largely on ability to associate the type, the host and the pathologic activity. Individual types had their select hosts and usually their specific pathologic activity. It was doubtful whether serologic factors were a reliable guide. The difference in mode of action was probably associated with difference in host resistance or degree of sensitivity of the animal intestine.

Mr. E. R. Lovell dealt with salmonella infections in domestic animals. In addition to sporadic infections there were several well defined conditions, such as bacillary white diarrhea of chickens, infections of bovines with Bacillus enteritidis and of mares and ewes with Brucella abortus and Brucella abortus ovis respectively. Salmonella bacteria were also found in frequent association with certain viruses, such as the virus of swine fever. Some of the less common varieties of Salmonella originally found in man were found to grow in animals, such as the pig. Until recently the Bacillus paratyphosus B organism was considered to be wholly human, but in Norway it was isolated from carriers and the source appeared to be a dog that was ill with vomiting and diarrhea just before the human cases developed.

Throat, Nose and Ear Hospitals

London has three hospitals devoted to diseases of the throat, nose and ear. There are also of course departments for these diseases in the large general hospitals. The two larger of the hospitals for these diseases—the Central London Throat, Nose and Ear Hospital and the Golden Square Nose, Throat and Ear Hospital—have decided to amalgamate. The committees of the two hospitals have agreed to erect on the enlarged site of the former, Gray's Inn Road, a hospital which should be the authoritative center of laryngology and otology of the British Empire. But the war has caused a postponement of building operations.

Canadian War Hospital in England

The Canadian Red Cross Society is providing funds to create in England for the Canadian wounded one of the most modern hospitals in the world. This hospital, which will have 660 beds, is taking shape at Cliveden, the seat of Lord Astor. It is hoped that the first section will be opened next month. All the departments will be equipped with the latest apparatus. The research laboratory will be under the supervision of a famous Canadian, Sir Frederick Banting, the discoverer of insulin. The Canadian Red Cross Society is doing important work in other directions at its overseas headquarters in London. An information and research bureau has been formed, where arrangements have been made for keeping records of all casualties among Canadian soldiers.

Woman Surgeon Loses Her Post in Consequence of Marriage

The unusual case of a woman surgeon who lost her post as visiting surgeon because she married came up at the annual meeting of the governors of the Glasgow Royal Samaritan Hospital for Women. She joined the staff in 1936 and was promoted visiting surgeon to fill a vacancy. Her appointment was terminated last September. An explanation was offered on behalf of the governors by the chairman, who declared that there was no ban on the appointment of a married woman to the staff. The decision not to renew the appointment of the woman surgeon was due to her marriage with another visiting surgeon. There were only three visiting surgeons, and the governors came to the conclusion that it was not in the interests of the hospital that a husband and wife should concurrently hold two out of the three posts. It was a delicate administrative point.

ITALY

(From Our Regular Correspondent)

April 1, 1940.

Congress of Obstetrics and Gynecology

The thirty-sixth Congress of the Società Italiana di Ostetricia e ginecologia was held at Turin, with Professor Cova as president. The first official topic was gynecologic symptoms of extragenital diseases. Professor Vozza, of the University of Cagliari, said that nutritional disorders may cause symptoms of genital disturbances. An insufficient diet, working in closed environment and the preoccupations of modern life have unfavorable influence on the genital functions of women. Tuberculosis, syphilis, chronic lead poisoning and argyria may cause ovarian insufficiency, dysmenorrhea, genital infantilism and sterility. Genital hemorrhages are frequent in industrial poisoning from arsenic, benzene and phosphorus.

With regard to the second topic, ovarian hormone therapy in obstetric conditions and in gynecologic diseases, Professor Maurizio, of the University of Sassari, said that estradiol monobenzoate is five times more active than estrone. It is advisable to establish an international unit of benzoate measured in milligrams. The ratio of doses between the parenteral, oral and percutaneous routes is 1:5:7. When the substance is administered by the intravenous route an immediate strong reaction follows. Estrogen and progesterone, when administered in primary amenorrhea, induce development of the mucosa and appearance of menstruation. Estrogen and progesterone therapy when administered in secondary amenorrhea, gives satisfactory results in 75 per cent of the cases if the condition is of less than one year's duration and in 30 per cent of the cases if it has existed for more than one year.

Professor Robecchi discussed the x-ray aspects of female sterility. The speaker carried on x-ray observations for sterility in more than 500 women. Sterility is caused in from 25 to 40 per cent of the cases by obstruction of the fallopian tubes with predominant location at the ampullar portion of the tubes.

Professor Clivio, of Genoa University, discussed the harmful effects of anticonceptional practices. Sometimes fibromuscular tumors develop late in the life of women who have resorted to anticonceptional methods.

The next congress will be held in Naples. The official topics will be etiopathogenesis of renal diseases during pregnancy, and obstetrics in Italian colonies. Professors Musazza and Gaifami will be speakers.

Public Health in Libya

The number of health institutions in Libya before the Italian occupation was as follows: a military and a municipal hospital of fifty beds each, a leprosarium and a pharmacy in Tripoli, a military hospital and a pharmacy in Bengasi and a pharmacy in Derna. There were also some private health institutions. Public health at present is a duty of the government in collaboration with a colonial council and a central inspectorial department. Each province has an office of sanitation with a medical inspector. A department in Tripoli supplies gratuitously with sanitary material all the health institutions of the provinces. Tripoli has an isolation hospital, a quarantine station and a laboratory of hygiene and prevention of diseases. Similar institutions are already functioning in Bengasi. The main cities have been provided with a hospital and the municipalities with centers for temporary care of patients. Trachoma is frequent among natives (75 per cent in native soldiers and 2 per cent in European soldiers). Among school children there is a frequency of 78 per cent for Moslems, 34 per cent for Jews and 3 per cent for Europeans. Several centers for free medical care of poor pregnant women, an organization for the care of parturients in their homes, a center for free distribution of milk, a dining room for poor mothers and a nursery for children of working mothers with free feeding for children are available. There is an organization of metropolitan midwives and a nursery school for Moslem women.

Personal

Professor Omodei-Zorini of the University of Rome was appointed to the chair of phthisiology of Naples University. The chair was recently established by the minister of national education. This is the second chair of phthisiology in Italy.

SWITZERLAND

(From Our Regular Correspondent)

April 12, 1940.

Number of Swiss Physicians

The official body of the Swiss medical profession has recently made its report for 1938. Inclusive of hospital physicians, the number of men actively engaged is 4,734, one physician to 882 persons out of a total population (1937) of 4,176,400 inhabitants. There were 3,488 practicing physicians, 1,521 of whom were specialists (44 per cent). Head physicians of hospitals numbered 170, with 963 paid and unpaid assistants. One hundred and thirteen physicians were employed in hygiene, on boards of health, as school physicians and so on. In the five Swiss universities, 1,531 medical students of Swiss nationality were enrolled during the winter semester of 1938-1939.

Charlatanism

Public health in Switzerland is not under federal control but is left to cantonal jurisdiction. This varies widely. In the small canton of Appenzell Ausser-Rhoden, for example, no requirement of medical training and examination for the practice of medicine exists. This canton has about thirty physicians and 180 "naturopaths" (naturärzte). One of these recently, on the occasion of his fiftieth birthday, distributed throughout Switzerland 50,000 copies of a pamphlet which he entitled "God helps him who helps himself." On the title page 777 diseases were alphabetically listed with 1,366 natural remedies. The diseases included cancer, mental debility, glaucoma, impotence, syphilis and poliomyelitis.

The intercantonal drug control bureau in Berne brought to the attention of the cantonal bureau the unscrupulous way in which human diseases were exploited and requested that the man be put out of business. He was tried before the cantonal court and acquitted. An upper court reversed the ruling but passed only a light sentence on the defendant, consisting of a four day imprisonment and a six month forfeiture of civic honors and rights. The case was appealed to the federal supreme court. It affirmed the lower court's decision, criticizing fraud in advertising.

Swiss Hospitals

The Swiss statistical bureau with the aid of the medical profession has prepared statistical data that include all public and private hospitals of Switzerland. There are 544 hospitals with

59,871 beds, 143 to 10,000 inhabitants, and 1,541 hospital physicians, 1,216 of whom have been appointed by the central bureau. There are 9,696 nurses, 7,969 of them females. About 10,000 persons are employed in the care and maintenance of patients and hospitals. Eighty-seven per cent of the beds are intended for adults, 13 per cent for children and infants. A total personnel of 100, including nurses, administrative and maintenance divisions, is required, on the average, for 300 beds (in children's hospitals and 361 in those of mental diseases). The distribution of the 544 hospitals and the 59,871 beds is given in the accompanying table. The total average use of hospital beds, allowing for individual variations, amounted to 80 per cent (94.3 per cent in hospitals for mental diseases). Hence hospital needs in normal times are sufficiently provided for.

During the year 1937 about 48,000 persons were hospitalized, with an average stay of fifty-one days. This relatively high

Distribution of Hospitals and Beds

	Hospitals, per cent	Beds, per cent
General hospitals (cantonal, district, circuit and community)	28.8	33.9
Hospitals exclusively for women	2.9	2.7
Hospitals exclusively for children	3.5	2.5
Tuberculosis sanatoriums	22.3	13.2
Hospitals for mental diseases	12.5	29.0

number is accounted for by the longer hospitalization of the mentally diseased, tuberculous and chronic patients. Though the proportion of females to males in Switzerland's population is high (108:100), the proportion of female to male patients (129:100) is exceptionally high. The mortality of hospitalized patients in relation to the total number of patients treated was 5 per cent. Of 1,000 deaths, 365 occur in the hospital.

More single rooms, however, are needed. Of the total of 59,871 beds, 31.7 per cent are situated in rooms intended for one and two beds, 36 per cent in rooms intended for from three to six beds, and 32.1 per cent in rooms of from seven to twenty-one and more beds.

THE NETHERLANDS

(From Our Regular Correspondent)

March 16, 1940.

Nutrition Problems in the Netherland Indies

In an article in the *Geneeskundig tijdschrift voor Nederlandsch-Indië* Prof. W. F. Donath, J. H. De Haas and G. J. A. Terra discuss the difficulties of improving the general nutrition in the Netherland Indies. In certain regions undernourishment exists because of a deficiency in the caloric values and in the quantity of animal and vegetable proteins, fats, mineral salts and vitamin A. A vitamin B deficiency is also encountered, although in general, where rice is the principal commodity of food, enough of the outer coat of the grain is left in the processing. The authors propose that studies be made to promote knowledge of the deficiency factors involved. They suggest the need of closer cooperation among existing agencies, such as the departments of public health and of the interior, of economic control and of education, a cooperation entrusted to the Institut pour l'alimentation populaire, which was founded in 1934 and subsidized from Queen Wilhelmina's jubilee foundation and by voluntary contributions. The work is at present done by seven scientific research groups, which are independent of one another.

The creation of an independent governmental research and laboratory institute, forming part of the public health service and possessing the power to initiate measures, is also regarded as desirable in the attack on the nutrition problems. The article lists 300 relevant publications that appeared between 1851 and 1936.

Malaria Control in North Brabant

Malaria control in the province of North Brabant is exercised from new epidemiologic points of view under the direction of Professor Swellengrebel. The guiding principles that seem to promise results consist in (1) destruction of mosquitoes by vaporizing insecticides between August 15 and the end of September, especially in houses in which large families are domiciled; (2) examination of the spleen of school children in infected regions in the search for plasmodia; (3) the administration of a plasmochin and quinine preparation three weeks before the danger period, that is, before anopheles begin to fly, and (4) the draining of polders.

Better Control of Rickets

Prof. E. Gorter has directed attention to the fact that, in spite of the discovery of vitamin D and the knowledge of its therapeutic use, the occurrence of rickets has not yet become exceptional in the Netherlands. Certain physicians, he says, do not think that vitamin D is prophylactically indicated and await the first manifestations of rickets, in spite of the fact that even the slight appearance of the disease is dangerous. On the other hand, the contracts of insurance companies do not provide for products containing vitamin D or for cod liver oil prescribed for nurslings. Nor are all infants duly examined. Reduction in the price of vitamin D preparations, irradiation of milk and the injection of vitaminized oil are not sufficient. The future must solve the problem.

Food Control

By ministerial decree, all contracts are to be cancelled and replaced by new ones. Eleven provincial commissariats have been created. They are in charge of the local staffs needed to carry out the agricultural measures to be effected. A census has been taken of the live stock and farm products among farmers and depositories of certain products. A bureau for wheat purchases has also been established. Plans have also been made for the transportation and distribution of foodstuffs in the event of hostilities.

The Inventor of Plaster Bandages

A statue is planned for Dr. Anthonius Mathysen, who invented the plaster bandage in the treatment of fractures. In 1855 he read a paper before the Academy of Medicine of Paris in which he explained the technic. It received the gold medal at the Philadelphia World's Exposition twenty-one years later.

Marriages

JESSE TROUSDALE FUNK, Bowling Green, Ky., to Maydelle Johnson Vandiver of Lexington in April.

ROBERT ANDREW HINGSON, Rochester, Minn., to Miss Gussie Dickson of Fitzgerald, Ga., March 2.

OWEN G. MCDONALD, Medford, Wis., to Miss Lois Gray of Kankakee, Ill., in Chicago in April.

ALBERT D. FROST, Columbus, Ohio, to Mrs. Martha White Craig of New York in March.

ROBERT C. BERSON, Ripley, Tenn., to Miss Marian Fairbanks Agry of Rye, N. Y., April 13.

GLENN E. STAYER to Miss Marion Henderson, both of Tampa, Fla., at Bradenton in March.

ALFRED SEYMOUR SCHWARTZ to Miss Ellen Jane Freund, both of St. Louis, May 5.

JAMES A SMRHA to Miss Lillian Jamesson, both of Cedar Rapids, Iowa, April 25.

ROBERT J. LEWIS to Miss Marguerite Blackwell, both of Indianapolis, recently.

SHIRLEY CARTER FISK, New York, to Miss Mary Averell Harriman in April.

Deaths

Rufus E. Fort, Nashville, Tenn.; University of Nashville (Tenn.) Medical Department, 1894; member of the Tennessee State Medical Association; fellow, and member of the board of governors from 1915 to 1933, of the American College of Surgeons; vice president and medical director of the National Life and Accident Insurance Company; past president of the state board of health; superintendent and chief surgeon, Nashville General Hospital, from 1893 to 1903 and later visiting gynecologist and abdominal surgeon; visiting surgeon and chairman of the executive committee of the Nashville Protestant Hospital; aged 68; died, March 22, in the Vanderbilt Hospital of coronary occlusion.

Lewis Harvie Taylor ✠ Washington, D. C.; Columbian University Medical Department, Washington, 1903; assistant professor of surgery, George Washington University School of Medicine, from 1906 to 1910; past president of the American Therapeutic Society; served during the World War; formerly attending surgeon on the staff of the George Washington University Hospital and the Casualty Hospital; consulting surgeon to St. Elizabeths Hospital and member of the board of visitors; president and superintendent of the Sibley Memorial Hospital from 1936 to 1940; aged 64; died, March 30, at Chula, Va., of coronary occlusion.

Porter Stiles, Dillwyn, Va.; Jefferson Medical College of Philadelphia, 1915; member of the American Academy of Ophthalmology and Otolaryngology and the American Broncho-Esophagological Association; fellow of the American College of Surgeons; served during the World War; formerly bronchoscopist and laryngologist to the Hillman Hospital, St. Vincent's Hospital and the South Highlands Infirmary and bronchoscopist to the Children's Hospital, Birmingham, Ala.; aged 49; died, March 23, in the Veterans Administration Facility, Kecoughtan.

Zabdiel Boylston Adams ✠ Boston; Harvard Medical School, Boston, 1903; member and in 1929 president of the American Orthopedic Association; formerly instructor of orthopedic surgery at his alma mater and associate in anatomy; served during the World War; at various times on the staffs of the Boston Children's Hospital, Massachusetts General Hospital, Boston and the Lakeville State Sanatorium, Middleboro, Mass.; member of the board of associate editors of the *Journal of Bone and Joint Surgery*; aged 65; died, March 16.

Hugh Halsey, Montclair, N. J.; College of Physicians and Surgeons, Baltimore, 1886; member of the Medical Society of the State of New York; past president of the Associated Physicians of Long Island; for many years health officer of Southampton, N. Y.; aged 75; died, March 21, of heart disease, shock due to fall down the stairs, arthritis and arteriosclerosis.

Joseph Loyd Golly ✠ Rome, N. Y.; Syracuse University College of Medicine, 1908; past president of the Oneida County Medical Society; fellow of the American College of Surgeons; surgeon to the Rome Hospital and Murphy Memorial Hospital; consulting surgeon to the Marcy State Hospital, Marcy, N. Y., and the Rome State School; aged 53; died, March 17.

Harriet L. Doane, Pulaski, N. Y.; Syracuse University College of Medicine, 1896; past president of the Woman's Medical Society of New York; for many years member of the board of visitors of the Marcy (N. Y.) State Hospital; aged 67; died, March 11, of chronic articular rheumatism and fracture of the vertebrae due to a fall.

John Lealand Taylor, Montezuma, Iowa; State University of Iowa College of Medicine, Iowa City, 1902; member of the Iowa State Medical Society; past president of the Poweshiek County Medical Society; county coroner; member of the city council; aged 67; died, March 14, of injuries received in an automobile accident.

Charles Ernest McLean, Toronto, Ont., Canada; M.B., Queen's University Faculty of Medicine, Kingston, 1912, and M.D., 1914; served during the World War; medical health officer for East York township, and county coroner for many years; aged 50; died, March 17, in the Toronto East General Hospital.

Amalie Marie Napier, St. Louis; Barnes Medical College, 1908 and 1909; member of the Missouri State Medical Association; formerly assistant in clinical ophthalmology at the Washington University School of Medicine; aged 73; died, March 16, at the Lutheran Hospital of lobar pneumonia.

Horace Duane Price, Parkersburg, W. Va.; Miami Medical College, Cincinnati, 1882; member of the West Virginia State Medical Association; at one time assistant superintendent of the Spencer (W. Va.) State Hospital; aged 82; died, March 24, of influenza and bronchopneumonia.

Samuel Lorenzo Stevens, Dalton City, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; member of the Illinois State Medical Society; served during the World War; aged 65; died, March 31, of chronic cardiovascular disease.

Edward Jenner Barrett, Sheboygan, Wis.; Cincinnati College of Medicine and Surgery, 1895; member of the State Medical Society of Wisconsin; veteran of the Spanish-American and World wars; aged 70; died, March 9, of coronary embolism and arteriosclerosis.

Sydney Elihu La Van Jr., New Haven, Conn.; University of Arkansas School of Medicine, Little Rock, 1939; aged 25; intern at the Hospital of St. Raphael, where he died, March 5, of pulmonary embolism following acute appendicitis with appendectomy.

George Edward Butler ✠ Fall River, Mass.; Bellevue Hospital Medical College, New York, 1896; served during the World War; on the staffs of the Union, St. Anne's and the Fall River General Hospital; aged 70; died, March 8, of coronary thrombosis.

Laurence Edwin Cooley ✠ Dubuque, Iowa; University of Minnesota Medical School, Minneapolis, 1928; served during the World War; formerly clinical assistant in medicine at Rush Medical College, Chicago; aged 39; died, March 26, of melanoma.

Lida Osborn ✠ Mankato, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1900; on the staffs of the Immanuel and St. Joseph's hospitals; aged 64; died March 11, of arteriosclerosis, hypertension and cerebral hemorrhage.

Frank C. Ainley ✠ Los Angeles; Johns Hopkins University School of Medicine, Baltimore, 1906; fellow of the American College of Surgeons; aged 60; on the staff of the Good Samaritan Hospital, where he died, March 16, of cerebral thrombosis.

Fred Henry Stangl ✠ St. Cloud, Minn.; Rush Medical College, Chicago, 1919; member of the American Society of Clinical Pathologists; aged 46; on the staff of St. Cloud Hospital, where he died, March 19, of subacute bacterial endocarditis.

William Samuel Hayling, Trenton, N. J.; Howard University College of Medicine, Washington, D. C., 1923; aged 55; died, March 19, in the Mercer Hospital of bronchopneumonia following suffocation when his mattress caught fire.

John Lee Grant, Winchester, Va.; George Washington University School of Medicine, Washington, D. C., 1907; formerly a minister; aged 65; died, March 21, in the Memorial Hospital, of cerebral hemorrhage with hemiplegia.

Leonard Fisk Wilbur ✠ Taiku, Shensi, China; Stanford University School of Medicine, San Francisco, 1932; an Associate Fellow of the American Medical Association; medical missionary; aged 33; died, March 24, of typhus.

Selden Talcott Kinney ✠ South Amboy, N. J.; New York Homeopathic Medical College and Flower Hospital, New York, 1911; on the staff of the South Amboy Memorial Hospital; aged 56; died, March 31, of chronic myocarditis.

Henry Aretas Barclay, San Diego, Calif.; Denver and Gross College of Medicine, 1906; member of the California Medical Association; veteran of the Spanish-American and World wars; aged 70; died, January 24.

William Griffin Hoyt, Mount Tremper, N. Y.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1882; aged 83; died, February 29, of cerebral hemorrhage and arteriosclerosis.

William G. Woodard, Oklahoma City; Vanderbilt University School of Medicine, Nashville, Tenn., 1888; also a druggist; formerly member of the state legislature; aged 78; died, March 30, of cerebral hemorrhage.

James Wallace Campbell, Gastonia, N. C.; College of Physicians and Surgeons, Baltimore, 1893; member of the Medical Society of the State of North Carolina; aged 69; died, March 20, of carcinoma of the liver.

Barnett H. Sirott ✠ Perth Amboy, N. J.; Fordham University School of Medicine, New York, 1915; on the staff of the Perth Amboy General Hospital; aged 57; died, March 24, of hypertension and arteriosclerosis.

Eugene Spencer Clark, Clarkton, N. C.; Medical College of Virginia, Richmond, 1914; member of the Medical Society of the State of North Carolina; aged 51; was killed, March 11, when struck by an automobile.

John Wesley Dixon, Burlington, Iowa; Trinity Medical College, Toronto, Ont., Canada, 1890; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1890; aged 75; died, March 26, of myocarditis.

Josiah S. Wheeler, Tishomingo, Miss.; Hospital College of Medicine, Louisville, 1898; member of the Mississippi State Medical Association; aged 75; died, March 27, of cerebral hemorrhage and hypertension.

Emma L. Braunwarth ✠ Muscatine, Iowa; State University of Iowa College of Medicine, Iowa City, 1881; an Affiliate Fellow of the American Medical Association; aged 81; died, March 1, of lobar pneumonia.

George Burton Wade ✠ Laingsburg, Mich.; Baltimore University School of Medicine, 1892; for many years member of the board of education; aged 76; died, March 28, of angina pectoris and arteriosclerosis.

Vernon Eugene De Grofft, Swedesboro, N. J.; Medico-Chirurgical College of Philadelphia, 1899; formerly mayor; served during the World War; aged 62; died, March 12, in the Cooper Hospital, Camden.

Horace Stokes Zernow, Delray, Fla.; University of Louisville (Ky.) Medical Department, 1908; aged 55; was killed, March 26, when the automobile in which he was driving was struck by a train.

Edward Louis Rohlf, Waterloo, Iowa; Omaha Medical College, 1900; member of the Iowa State Medical Society; served during the World War; aged 71; died, March 6, of cerebral hemorrhage.

Joseph Philip Evans ✠ Chicago; Loyola University School of Medicine, Chicago, 1930; clinical assistant in medicine at his alma mater; aged 38; died, March 21, at Rochester, Minn., of glioma of the brain.

Robert A. Kennedy, Cleveland; Western Reserve University Medical Department, Cleveland, 1888; aged 78; died, March 13, of carcinoma of the lung with metastases to brain and vertebrae.

Singleton Starr Smith, Athens, Ga.; Atlanta Medical College, 1892; member of the Medical Association of Georgia; past president of the Clarke County Medical Society; aged 70; died, February 18.

Harry Henderson Steinmetz ✠ Manila, P. I.; Kentucky University Medical Department, Louisville, 1906; past president of the Philippines Islands Medical Association; aged 61; died, February 28.

Leslie Adams Wilson ✠ Meriden, Conn.; Yale University School of Medicine, New Haven, 1910; on the staff of the Meriden Hospital; aged 53; died, March 15, of coronary thrombosis.

Kenneth Sylvan Launfal Guthrie, Keansburg, N. J.; Medico-Chirurgical College of Philadelphia, 1904; also a clergyman; aged 68; was killed, March 17, when struck by an automobile.

Richard Benbridge Wetherill ✠ La Fayette, Ind.; Jefferson Medical College of Philadelphia, 1883; fellow of the American College of Surgeons; aged 81; died, March 27, of pneumonia.

James George Flynn ✠ Ridgway, Pa.; College of Physicians and Surgeons, Baltimore, 1901; on the staff of the Elk County General Hospital; aged 63; died, March 5, of arteriosclerosis.

Elisha Herman Liston, Nevada, Mo.; Illinois Medical College, Chicago, 1898; member of the Missouri State Medical Association; aged 69; died, March 29, of atrophic cirrhosis of the liver.

Junius Taylor Ireys, Greenville, Miss.; University of Pennsylvania Department of Medicine, Philadelphia, 1900; aged 64; died, March 31, of chronic interstitial nephritis and arteriosclerosis.

Floyd Everest Radcliffe ✠ Bourbon, Ind.; Medical College of Indiana, Indianapolis, 1898; past president of the Marshall County Medical Society; aged 63; died, March 15, of angina pectoris.

Timothy John Moynihan ✠ St. Paul; Minneapolis College of Physicians and Surgeons, 1906; aged 62; on the staff of the Midway Hospital, where he died, March 8, of cerebral hemorrhage.

Francis Marion Tindall, Sunflower, Miss.; University of Virginia Department of Medicine, Charlottesville, 1915; aged 53; died, March 31, in the King's Daughters' Hospital, Greenville.

Jay Gould Keiser, Bexley, Ohio; Cleveland Homeopathic Medical College, 1909; served during the World War; aged 55; died, March 29, of multiple sclerosis and lobar pneumonia.

James Adrian Conlan ✠ Pittston, Pa.; Jefferson Medical College of Philadelphia, 1931; on the staff of the Pittston Hospital; aged 36; was killed, March 26, in an automobile accident.

Austin W. Peppers, Birmingham, Iowa; Barnes Medical College, St. Louis, 1902; member of the Iowa State Medical Society; aged 61; died, March 8, of carcinoma of the prostate.

Charles Clarence Headley ✠ Cambridge, Ohio; Medical College of Virginia, Richmond, 1906; on the staff of the Swan Hospital; aged 61; died, March 28, of cerebral hemorrhage.

Louis Demme Bauer ✠ Philadelphia; Jefferson Medical College of Philadelphia, 1890; veteran of the Spanish-American War; aged 71; died, March 29, of coronary thrombosis.

Martin L. Brookshier, Georgetown, Ill.; Barnes Medical College, St. Louis, 1903; member of the Illinois State Medical Society; aged 62; died, March 22, of chronic asthma.

Julius Hauck, St. Louis; St. Louis University School of Medicine, 1912; member of the Missouri State Medical Association; aged 67; died, March 30, of heart disease.

Michael Pinckney Morrell, St. Louis; University of Virginia Department of Medicine, Charlottesville, 1873; aged 89; died, March 28, in the City Hospital, of uremia.

Gustav Paul Hoffmann, South Orange, N. J.; University of the City of New York Medical Department, 1894; aged 68; died, March 25, of carcinoma of the stomach.

Edwin Price Howell, Dickinson, Texas; Kansas City (Mo.) Homeopathic Medical College, 1899; aged 83; died, February 14, of carcinoma of the cervical glands.

Frank Pattillo Norman, Columbus, Ga.; Atlanta School of Medicine, 1910; member of the Medical Association of Georgia; aged 53; died, March 17, of myocarditis.

Joseph Mazurette Lapierre ✠ Rutland, Vt.; University of Montreal Faculty of Medicine, Montreal, Que., Canada, 1912; aged 55; died in March of pneumonia.

John Paul Peter Rajotte, Sorel, Que., Canada; University of Montreal Faculty of Medicine, Montreal, 1933; aged 33; died, March 19, of granulocytopenia.

Henry William Cox, Hot Springs National Park, Ark.; Bennett Medical College, Chicago, 1911; aged 73; died, March 22, of pulmonary tuberculosis.

William Arthur Garner ✠ Kiron, Iowa; Hahnemann Medical College and Hospital, Chicago, 1905; aged 62; died, March 27, of coronary sclerosis.

Julia Grice Kennelly, Cambridge, Mass.; Woman's Medical College of Pennsylvania, Philadelphia, 1900; aged 71; died, February 9, of heart disease.

Bruce Leon De Witt Cook, Buffalo; Niagara University Medical Department, Buffalo, 1898; aged 65; died, March 18, of coronary thrombosis.

Howard Johnson Combs, Elizabeth City, N. C.; Jefferson Medical College of Philadelphia, 1918; aged 45; died, March 30, of pneumonia.

Isaac Rich, New York; Long Island College Hospital, Brooklyn, 1906; aged 63; died, February 4, of pneumonia and diabetes mellitus.

James Harrison Murphy, Kansas City, Mo.; Rush Medical College, Chicago, 1885; aged 77; died, March 10, of uremia and arteriosclerosis.

Everett Mayhew Swift, New York; New York Homeopathic Medical College, New York, 1879; aged 88; died, March 19, of senility.

Moses Haynes, Bingham, Ill.; Missouri Medical College, St. Louis, 1877; aged 90; died, March 16, of intestinal obstruction.

Robert Lee La Rue, Eustace, Texas; Memphis (Tenn.) Hospital Medical College, 1909; aged 70; died, March 20, of pneumonia.

Homer J. Grant ✠ Buffalo; Albany (N. Y.) Medical College, 1892; aged 70; died, March 16, in the Buffalo General Hospital.

Adrien Filion, Montreal, Que., Canada; University of Montreal Faculty of Medicine, 1927; aged 39; died, March 11.

Bureau of Investigation

A "FAT CURE" FRAUD

Mails Are Closed to R. B. Macrorie's Scheme

An individual operating a mail-order "obesity cure" from Davenport, Iowa, under the names Mac Rory and R. B. Macrorie, followed the same tactics that others before him in the same field had employed: He decried all the other treatments and claimed that his was "different." Macrorie sold no "patent medicines" or devices and advocated no exercises, massages, bath salts, "melting creams," "reducing soaps" or the rest of the paraphernalia of the fat-cure quack. What then did he offer? Just diets!

When the Post Office Department looked into his "different" treatment for excess weight it found that he solicited business by advertising in newspapers and periodicals. One of his advertisements read:

> NEW Way to Reduce Fat Never FAILS. No drugs, rubs, exercise, baths, or starving. Harmless. Aids health. $1.00 complete. Every tenth dollar bill refunded. Mac Rory, Box 434, Davenport, Iowa.

Persons who answered Macrorie's advertisements received circulars in which he declared:

> All of the OLD [later on in the text he said "Most of the OLD"] methods of getting rid of surplus fat are expensive; many of them are dangerous; none are dependable . . .
>
> In my NEW method there are no drugs, no exercise, no massages, no baths, no weakening diets. The more one eats the quicker one reduces. The layers of fat next the skin and the layers covering the heart and internal organs disappear as the person becomes stronger, healthier, and more active. The fat does not return unless one intentionally puts it back on . . . Nature does the work as one eats heartily. There is no discomfort. Soon one regains the youthful figure without flabbiness and wrinkles. Think of that: The curves, energy, and activity of youth; the pleasures, the affectionate contacts of youth.
>
> My NEW method never fails to remove surplus fat. Not a single person has reported adversely. They removed 75, 100, 125 pounds or more without discomfort or expense, then maintained their figures and gained in health. My NEW method cannot cause illness.

The circular went on to say that the secret would be yours for $4—in fact, you could obtain it by sending only $2 at the start and paying the rest "when you have reduced." Macrorie assured you he would not even dun you for it.

Those trusting souls who duly sent the $2 received a printed sheet entitled "Weight Reduction and Control. Copyright 1938, by R. B. Macrorie." And what did it advise? Reduce by eating more! Not only of lean meats and "all vegetables" but "be sure to eat much starchy food, the more the better," but he also advised:

> Do NOT eat the following: Fried things, oils, salad dressings, butter, oleo, cheese, full milk, candy, chocolate, nuts, pies, cake or other pastries, olives, beer.

Apparently Macrorie did not know that "cake or other pastries" *are* "starchy food"!

There followed many paragraphs of dietetic advice, and finally a statement of what results to expect:

> Sample reductions: Male, 70 pounds in 4 months. Girth losses: Waist 10, chest 9, thighs 7, neck 1½, calf 2½ inches, shoes one size smaller. After reduction a gradual return was made to regular method of eating. The gentleman gained, in the following five years, exactly 6 pounds in all. He had no illness during or since.

On the other hand, Macrorie claimed that, if one wished to maintain a certain weight without loss or gain, "quite another method may be used . . . that is to cut down to two meals a day," namely, breakfast at noon and dinner in the evening—"both meals old-fashioned and greasy."

According to the memorandum issued on this case by Judge Vincent M. Miles, Solicitor for the Post Office Department, a chief objection to Macrorie's scheme was that though the man, before selling an individual the "secret," represented that his method involved no rigorous dietary restrictions, nevertheless after the victim had paid over his money he then learned that he was expected to eliminate from his diet "fried things, oils, salad dressings, butter, oleo, cheese, whole milk, candy, chocolate, nuts, pies, cake or other pastries, olives, beer." Furthermore, to obtain "quick" reduction of weight, he must limit himself to two meals a day.

The memorandum also brought out that the expert medical evidence presented had shown that obese persons are of two principal types—those whose overweight is due to excessive eating, usually but not necessarily accompanied by insufficient exercise, and those whose obesity is caused by disturbances of the endocrine glands. In the first type any substantial reduction in weight can result only from a lowering of the daily food and caloric intake and the ability of the body to burn its accumulated fat. Hence no reduction could be accomplished by following the advice to "eat freely of bread and potatoes" and to "be sure to eat much starchy food, the more the better," nor could a fixed weight "without loss or gain" be uniformly maintained if the two meals a day recommended for this were to be "old fashioned and greasy" and the dinner a "very hearty one," as Macrorie recommended.

Though the second type of obesity—that due to hyperthyroidism—is not controllable by diet but must be treated according to the patient's individual needs, nevertheless it was shown that in at least one instance Macrorie had sold his method on representations that it *would* reduce the weight of a person whose obesity was due to hyperthyroidism.

The medical evidence further brought out that though the Macrorie method would not and could not bring about a reduction of "75, 100, 125 pounds or more," as promised in the literature, such reductions even if accomplished would result not only in flabbiness and wrinkles as the affected tissues underlying the skin were eliminated, but also in lowered strength and vitality, with consequent susceptibility to illness and infections on the part of the subject.

After considering these facts and others that need not be gone into here, the Solicitor found that Macrorie's business was a scheme for obtaining money through the mails by means of false and fraudulent pretenses, representations and promises, and on his recommendation the Post Office Department issued a fraud order on Sept. 19, 1939, against the names Mac Rory and R. B. Macrorie.

"HERBOLA-HINDU HEALTH HERBS" HOKUM

Post Office Department Finds This a Fraudulent Scheme

Kaleas Chowdhury, also known as Kaelas Choudhury, a native of Calcutta, India, introduced to the public his "Herbola-Indian Health Herbs" and "Eetola." Chowdhury, who is said to have resided in the United States for over thirty years without becoming naturalized, conducted his nostrum business from Gary, Ind., under the high-sounding names Aryan Herb Company and Aryan Herb Tonic Company.

The first government agency to look into the activities of this outfit was the Food and Drug Administration, which seized consignments of Eetola that had been shipped in interstate commerce in May and December 1937. Government chemists reported that their analysis of a specimen showed it to consist essentially of extracts of plant drugs including hydrastis; volatile oils including those of sandalwood and cubeb; balsam copaiba, and water. The government charged that the label fraudulently represented that Eetola would cure chronic gonorrhea, stricture, prostate trouble, bladder and urethral infections, white and yellow discharge, burning urination, pain under the abdomen of men and women, kidney infection and "weak manhood"; and that it was a scientific preparation of tonic efficacy. At the hearing of this case in November 1938, Chowdhury entered a plea of *nolo contendere* and was fined.

Around this time, the Post Office Department also was investigating the outfit and its preparations—Eetola, Herbola and a so-called tea—which were being sold through the mails under representations that they would reduce high blood pressure to normal and overcome numerous other ailments, including kidney and bladder disorders, all kinds of female troubles, lost sexual vigor, rheumatism, stomach and liver complaints, and some other things.

The memorandum on the case, submitted by Hon. Vincent M. Miles, Solicitor for the Post Office, brought out that Chowdhury had started the business in 1928 and had reached the public by means of newspaper and magazine advertisements directed, for instance, toward "men over 30 with burning urine—no pep or

vigor" or "Sweet Sixteen or Women Up to Fifty, suffering from periodic or constant pains over the ovaries . . ." The "formulas" that Chowdhury was reported to have given for Herbola and Eetola included lists of common herbs too numerous to take up space here. It may be said, however, that they suggested the old "shotgun" type of nostrum.

According to the memorandum, analysis of Herbola by the government chemists showed that, in addition to the ingredients declared by Chowdhury, it contained 14.80 grains of epsom salt per hundred cubic centimeters and that a "tea" sold in connection with it was composed of powdered black haw and watermelon seed.

The Solicitor's memorandum also brought out that expert medical evidence had been presented to show that the various disorders for which Chowdhury's nostrums had been sold were not curable by these laxative and diuretic mixtures, and he recommended that the business be debarred from the use of the mails. Accordingly a fraud order to that effect was issued by the Post Office Department on Sept. 14, 1939, against Aryan Herb Company, Aryan Herb-Tonic Company, Aryan-Herb Tonics Company, Miss Stuart, Miss R. Stuart, R. Stuart, R. Stuart, Secretary, and their officers and agents as such—but the name of Kaleas Chowdhury was not included!

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SWIMMING POOLS

To the Editor:—**We are endeavoring to obtain a municipal swimming pool in our community and there seems to be some opposition from the point of view of health. Is this opposition justifiable? What methods of purification are used in modern pools? Which is the best? How effective are they? What is the possibility of transmitting disease, including venereal disease? How can it best be avoided?**

John T. Hecker, M.D., Cedar Rapids, Iowa.

ANSWER.—The modern swimming pool with proper management and operation affords as safe and sanitary a place to swim as can be found anywhere. Sanitation of the modern concrete or tile swimming pool is based on the same principle as sanitation of the supply of drinking water for cities which have a water supply that is originally polluted. This consists of filtration through a set of pressure or gravity filter tanks and treatment of the water with the proper amount of chlorine or ammonia or both. The use of chlorine plus ammonia forms chloramine, which is practically nonirritating to the eyes, renders the chlorine more stable in the water when exposed to the sun and air, tends to prevent the growth of algae and permits the use of smaller amounts of chlorine in the water. The water in the modern pool can be kept at drinking water standards of purity. Purification of the water may also be accomplished by the use of sodium hypochlorite. Purification by the use of ultraviolet rays, ozone or a silver electrolytic system were methods used in the past, the effectiveness of which has been the subject of debate. It is important that a municipal pool be under proper management and that simple regulations regarding hygiene, the use of foot baths of sodium hypochlorite to prevent development of ringworm, athlete's foot, and the like be employed. (Montgomery, Hamilton: The Modern Swimming Pool: Its Sanitation and Safety, *Proc. Staff Meet., Mayo Clin.* **11**:561 [Sept. 2] 1936, and the annual manuals issued by *Beach and Pool* magazine, which gives rules and regulations regarding swimming pools, instruction and maintenance of pools, and other information.)

There is no danger of transmission of a venereal disease in the pool. Proper sanitation of toilets is obviously necessary. Certain individuals may develop infection in the ear through forcing bacteria up the eustachian tube. These individuals or those with open ear drums have to be warned against the danger of diving. No endemics of respiratory infections appear to have been reported from a properly designed and operated municipal pool.

GOLD SODIUM THIOSULFATE IN ARTHRITIS

To the Editor:—**Please advise me as to the use of gold sodium thiosulfate in the treatment of arthritis. Is there any particular brand or preparation on the market that is considered the best to use?** **M.D., Illinois.**

ANSWER.—Many physicians in France believe that chronic arthritis is etiologically related to tuberculosis, a view which is not accepted in this country. Working on this assumption Forestier in 1929 began to use gold salts in the treatment of atrophic (rheumatoid, infectious, proliferative) arthritis. In 1934 he reported that from 70 to 80 per cent of 500 patients treated had been distinctly improved. Since then many other workers, particularly in France and England, have reported good results in a significant percentage of cases. The use of gold salts (chrysotherapy) has been called "the best single form of treatment now available," but its great drawback is that toxic reactions to the gold are common, occasionally serious or even fatal.

Many preparations have been used. No preparation is notably safer than others. Some of the preparations are given intramuscularly, others intravenously; oral preparations are ineffective. Injections generally are given every four to seven days; the dose is increased gradually from an initial dose of about 10 or 15 mg. to a maximal single dose of 50 or 100 mg. The usual total dosage for one course is 1 Gm. One course is inadequate. Two or more courses generally are given, with an interval of six to twelve weeks between. The scheme of Ellman and Lawrence is somewhat different from that used by others: the size of succeeding doses and the length of each course were determined not more or less arbitrarily, as in other schemes, but by the patient's changing clinical condition and sedimentation rate.

Toxic reactions are unfortunately frequent and are varied in type. Since most of the gold is excreted by the kidneys and the rest by the intestine, toxic reactions especially affect the kidneys, stomach and intestine. The following reactions may occur: temporary increase in articular pain, rashes of various sorts, papular eruptions, edema, even exfoliative dermatitis, stomatitis, conjunctivitis, iritis, "gold bronchitis," gastro-enteritis of variable degrees including hepatitis with jaundice, albuminuria, occasionally acute nephritis, and various psychic and neurologic reactions. Most important of all are the effects on the hematopoietic system: reduction in number of leukocytes and platelets, aplastic anemia, granulocytopenia and purpura haemorrhagica, any of which may be fatal.

Of patients treated with gold salts about 50 per cent or more do not have toxic reactions. Toxic reactions of about 15 per cent of patients given gold salts are mild, those of about 10 to 20 per cent are moderately severe, of about 6 per cent severe but not fatal, and 1 per cent or less have fatal reactions. Several physicians have treated fifty or sixty patients or less without a fatality, but those who have treated larger numbers (from seventy to 700) have reported fatal reactions in about 1 (0.8 to 1.4) per cent. To date no method for preventing or anticipating these toxic reactions has become established. Because of the type of reactions induced, chrysotherapy is contraindicated for patients with gross renal or hepatic disease, colitis, pregnancy, eczema, severe anemia or hemorrhagic tendencies, previous purpura or granulocytopenia, severe diabetes, hypertension or congestive heart failure. Old age, arteriosclerosis, moderate hypertension and psoriasis have not been considered contraindications. To discover the first signs of toxemia, careful management is required. This involves repeated clinical examination of the patient: urinalysis, differential blood counts and sedimentation rates. Recently Secher claimed that severe toxic reactions can be prevented or controlled by the use of large doses of vitamins A, B and C; his claims have not yet been substantiated.

Are the results worth the risk? British and continental workers believe they are; most American workers to date are inclined to believe they are not. It is agreed that gold salts are not effective in rheumatic fever, fibrositis, gout or hypertrophic (osteo-) arthritis. Their use in ankylosing spondylitis is considered valueless by most workers, of some value by others. Cures have been accomplished in an average of 10 per cent of foreign cases, in from 0 to 6 per cent of American cases. In addition, great relief has been afforded in from 50 to 70 per cent of foreign cases in which two or more courses of treatment were given, but notable relief has been noted in only about 10 to 35 per cent of American cases.

Because of these results and the risks involved, physicians should adopt a conservative attitude toward chrysotherapy for atrophic arthritis. The cause of relief is unknown and the method is empirical. It probably should be considered too dangerous for general use but worth trying in carefully selected cases. It should not be given to patients whose atrophic arthritis is obviously becoming inactive. It should be given only to those

patients whose disease is sufficiently severe and progressive to warrant taking the risk, to those unrelieved by an intensive trial, for a reasonable period, of more conservative methods, and to those who, with their close relatives, understand the risks involved and are psychologically prepared to take them and to share the physician's responsibility. Above all it should be applied only by physicians who have thoroughly familiarized themselves with the chief reports on chrysotherapy in order to learn the details necessary for its proper application. The Council on Pharmacy and Chemistry has not accepted any gold preparations for use in the treatment of either tuberculosis or arthritis.

References:

Copeman, W. S. C., and Tegner, W. S.: *Lancet* **1**: 554 (March 6) 1937; *Post-Grad. M. J.* **13**: 306 (Sept.) 1937.

Ellman, Philip, and Laurence, J. S.: Reports on Chronic Rheumatic Diseases, number 4, London, H. K. Lewis & Co., Ltd., 1938, pp. 121-148; *Post-Grad. M. J.* **14**: 275 (Sept.) 1938.

Forestier, Jacques: *Bull. et mém. Soc. méd. d. hôp. de Paris* **53**: 323 (March 11) 1929; *Lancet* **1**: 441 (Feb. 27) 1932; **2**: 646 (Sept 22) 1934; *J. Lab. & Clin. Med.* **20**: 827 (May) 1935.

Hartfall, S. J., and Garland, H. G.: *Lancet* **2**: 8 (July 6) 1935; **1**: 1459 (June 27) 1936.

Hartfall, S. J.; Garland, H. G., and Goldie, William: *Lancet* **2**: 784 (Oct. 2) 1937; **2**: 838 (Oct. 9) 1937; **2**: 1410 (Dec. 17) 1938.

Hench, P. S.; Bauer, Walter; Dawson, M. H.; Hall, Francis; Holbrook, W. P., and Key, J. A.: *Ann. Int. Med.* **12**: 1095 (Jan.) 1939.

Key, J. A.; Rosenfeld, Herman, and Tjoflat, O. E.: *J. Bone & Joint Surg.* **21**: 339 (April) 1939.

Sashin, David; Spanbock, Joseph, and Kling, D. H.: *J. Bone & Joint Surg.* **21**: 723 (July) 1939.

Secher, K.: *Lancet* **1**: 996 (April 30) 1938.

Snyder, R. G.; Traeger, Cornelius, and Kelly, LeMayne: *Ann. Int. Med.* **12**: 1672 (April) 1939.

Tegner, William: Reports on Chronic Rheumatic Diseases, number 3, London, H. K. Lewis & Co., Ltd., 1937, pp. 63-71; *Proc. Staff Meet., Mayo Clin.* **14**: 117 (Feb. 22) 1939.

SYNCOPE

To the Editor:—**Is there any connection between gastric upset and syncope? I had a patient, a man aged 29, who was a moderate indulger in alcohol and on two occasions while out for the evening after consuming 3 ounces of whisky, followed by a medium sized meal, felt ill and on going to the bathroom fainted. This was a bit unusual, for often this patient could take from one-half to 1½ pints of alcohol in an evening and suffer no ill effects. I might add that on the two occasions when syncope took place the patient had had a hard day previous to going out and was quite fatigued. What interests me most in this case is the possibility of the existence of some reflex phenomenon between the gastrointestinal tract and the central nervous system which would account for these attacks of syncope.**

M.D., Maine.

ANSWER.—There are at least three mechanisms which may act, either independently or in combination, to produce syncope: (1) reduction of the heart rate, (2) reduction of the general mean arterial pressure and (3) localized reduction of blood flow to the cerebrum. The presence of viscerocardiac reflexes has been demonstrated both in experimental animals and in man. Bachrach, Bonnet and Richard (*Ann. Physiol. Physicochem. biol.* **7**:192, 1931) and K. Wiggers (*Arch. néerl. de physiol.* **22**:558 [Dec.] 1937) produced cardiac inhibition by excitation of abdominal viscera. Tournade and Rocchiscani (*Compt. rend. Soc. de biol.* **115**:1637, 1939) reported a reflex hypotension from distention of the stomach. Bettman and Rubinfeld (*Am. Heart J.* **10**:550 [April] 1935) reported heart rate changes occurring in man when the gallbladder was manipulated during cholecystectomy. The production of syncope, however, through gastric reflexes has not been widely discussed in the literature. Weiss and Barker (*Medicine* **12**:297 [Sept.] 1933) in their study of the syncope produced by the carotid sinus reflex, suggest the possibility that there may be an extensive afferent vasodepressor mechanism in the body which may use the same efferent pathway as the carotid sinus reflex. Lewis (*Brit. M. J.* **1**:873 [May 14] 1932) also suggested that the syncopal mechanism "can be set in motion through many afferent channels other than those at present recognized by physiology." The former authors quoted the experimental work of Hatcher and Weiss (*J. Pharmacol. & Exper. Therap.* **22**:139 [Oct.] 1923) in support of their statement. These experiments indicated that (1) in the medullary reflex of nausea and vomiting a number of the same efferent pathways are involved as in the carotid sinus reflex, and (2) the same drug applied over the same area of the medulla produced different types of motor effects, depending on the state of the body. Crittenden, in Ivy's laboratory, gave apomorphine to unanesthetized animals and found (*Am. J. Physiol.*, Proc. **101**:26, 1932) that the heart rate was increased prior to the onset of vomiting but that just before and during the vomiting act the heart rate was markedly decreased. Other suggestive evidence is that of Gammon and Bronk (*Am. J. Physiol.* **114**:77 [Dec.] 1935), who report that the pacinian corpuscles lying adjacent to the mesenteric arteries discharge impulses in a manner somewhat resembling the carotid sinus end organs.

The data presented suggest that under certain circumstances reflexes from the abdominal viscera might operate to produce syncope. It is advisable, however, in a case of this kind to make a careful search for other conditions known to produce fainting spells, notably emotional upset, carotid sinus reflex, postural hypotension, neurocirculatory asthenia and petit mal.

LONG CONTINUED BILIARY OBSTRUCTION

To the Editor:—**About one year ago I performed a cholecystectomy on a white woman aged 35, following which she had an uneventful convalescence. About three months ago she became jaundiced and as time went on the icterus became progressively deeper and severe pruritus occurred. The liver was considerably enlarged and somewhat tender, and choluria and acholic stools seemed to indicate that an obstructive type of jaundice was present. After no improvement with conservative management I decided that surgery would be necessary for relief of an apparent extrahepatic biliary duct obstruction. One month ago a laparotomy was performed, and the common bile duct and hepatic duct were found enmeshed in adhesions and stenosed. The liver was found deeply bile stained and enlarged, and aspiration from the proximal portion of the hepatic ducts revealed a pale yellow fluid (white bile). A choledochotomy with insertion of a T tube into the ducts was performed. The patient has made a good convalescence from the operation and during the first two weeks drained considerable bile both through and around the tube from a stab wound in the flank. At present there is just scant drainage of still watery appearing bile. The stools show slight color, and less bile is present in the urine. The liver enlargement has gone down considerably. How much longer should I allow the tube to remain in situ, or what criteria should guide me in deciding on its removal? Also I would appreciate any suggestions as to the technic of removal of the tube other than simply teasing it out.**

J. M. Spatz, M.D., Glasgow, Mont.

ANSWER.—The long continued biliary obstruction has undoubtedly caused considerable liver damage, and the persistence of "a scant drainage of still watery appearing bile" suggests that there has not yet been complete recovery. Presumably at the time of the second operation the stenosis of the common duct was relieved and a free passage way into the duodenum secured. It would appear wise to leave the T tube in place for three or four months or until a free flow of normal appearing bile appears at the tube or the stools become normal in color and composition. The tube may then be clamped shut for several days and the patient observed for the reappearance of jaundice and the urine and stools examined for bile. In the interval the patient should be given orally a preparation of bile salts and vitamin K.

HAWTHORNE BERRY AND HYPERTENSION

To the Editor:—**What information can you give me in relation to the use of tincture of hawthorne from the hawthorne berry in the treatment of high blood pressure? Is it true that this preparation is efficent in hypertension? Has any work been done recently in this connection and can you give me any references?**

M.D., Illinois.

To the Editor:—**Could you furnish information relative to the use of hawthorne berries (Crataegus) for the treatment of hypertension? I would appreciate any literature that may be available on the subject.**

M.D., New Jersey.

ANSWER.—Tincture of hawthorne (Crataegus oxyacantha) is not recognized as a pharmacologically active preparation either by standard textbooks on pharmacology or by the Council on Pharmacy and Chemistry of the American Medical Association. A recent paper (Graham, J. D. P.: *Brit. M. J.* **2**:951 [Nov. 11] 1939) reports "encouraging" therapeutic results in ten cases of hypertensive disease followed for about six weeks. This is far too short a time and far too small a series of cases to warrant anything more than some hope that there may be possibilities with this preparation. Unfortunately this report has received some premature newspaper publicity through a health column. Graham himself is conservative in his conclusions. The tincture of crataegus had no effect in slowing the cardiac rate: it caused no diuresis in the decompensated patients. Large doses were ineffective on the normal arterial tension. There was no evidence of cumulative action; after cessation of medication the arterial tension returned to the previous levels. It was reported, however, that during the period of exhibition of the drug the arterial tension was maintained at a considerably lower average level than either before or after the medication. Despite this encouraging preliminary report it must be emphasized that a great deal more work and extensive clinical studies are necessary before the efficacy of such a drug can be evaluated. One should be skeptical, for there has been a long procession of medicaments advocated for the management of hypertensive disease. The usual sequence is that glowing preliminary reports are soon followed by more critical appraisals and with studies of better controlled clinical series it finally appears that the preparation is relatively useless. The iodides, preparations of mistletoe and of garlic, cucurbocitrin (watermelon seed glucoside, see report of the Council on Pharmacy and Chemistry,

THE JOURNAL, April 5, 1930, p. 1067), cobalt salts, calcium preparations and certain tissue extracts are among the many preparations tried, found wanting and finally discarded. It must not be forgotten that the intense enthusiasm of the original "discoverer" is often contagious. The psychotherapeutic effects of confidence in a "new discovery" may be a potent factor in inducing transient and misleading remissions, particularly in hypertensive disease, in which the psychosomatic factors loom large. Drugs are at best but auxiliaries in the management of hypertensive disease. Individualization is essential and the emotional and hereditary factors, together with the habits of the individual, usually need attention.

RADIATION AND ENDOCRINE GLANDS

To the Editor:—Several of my patients have been visiting New York and having treatments by endocrine experts, receiving among other things treatment with "gamma rays," which are generated by an x-ray machine or by radium. I understand that they are supposed to be a gland stimulant. I have been unable, either from my own knowledge or from other sources, to construe properly the meaning of this term and to define it.

G. F. Norman, M.D., San Francisco.

ANSWER.—True gamma rays are produced only by radium or radon. If the rays used in the treatment of the patients were not generated by radium they were not true gamma rays. From the information given, it would be impossible to guess what kind of rays they were or if they were rays at all. The only form of endocrine treatment involving the use of radiation therapy which has been used to any extent is for the relief of certain menstrual disorders. It is claimed that x-ray irradiation is of value in certain types of amenorrhea and menorrhagia. This treatment is not accepted by most gynecologists, although it is used by some. X-ray irradiation of the thyroid has a certain doubtful value; all other forms of irradiation of glands are most questionable. This includes irradiation of the pituitary for diabetes mellitus and of the adrenal for hypertension. The rare condition of basophilic adenoma of the pituitary is said to respond to x-ray irradiation with fair results. Many authorities consider that irradiation has only a destructive action on endocrine glands, not a stimulating one.

FAILURE OF EJACULATION AFTER PROSTATIC RESECTION

To the Editor:—A man aged 63, who has been well with a normal sexual life, had a transurethral resection of the prostate. The operation was entirely successful in the relief of the obstruction and control of the bladder, with apparently normal sexual desire as before operation. There has been entire absence of seminal fluid with ejaculation since. Is this the rule? If so, why. If not, what are your suggestions as to treatment?

M.D., Michigan.

ANSWER.—The result obtained in this case appears perfect—that is, the complete relief of obstruction. The patient has perfect control of the bladder and normal sexual desire. The entire absence of seminal fluid with ejaculation since the operation is not the rule; it is a rare exception. This may be due to several things: First, it is possible that the seminal fluid regurgitates back into the bladder and then evacuates with the urine. The way to determine whether or not this phenomenon is present is to have the patient bring in some urine after sexual intercourse. If this phenomenon does not occur, one must assume that occlusion of the ejaculatory ducts has taken place. This occurs in a small number of cases and it does no harm. There is no treatment to overcome this stenosis. In view of the fact that it does no harm, no treatment is indicated.

SMALL BREASTS

To the Editor:—In the case of a single girl in the early twenties with normal menstruation and normal development except for small breasts, would treatment with endocrine products such as progynon be of any value to promote development of the breast? Would massage be of any value? Further development is desired merely for cosmetic reasons, to look better in her clothes and so on. Do you have any other suggestions?

M.D., Iowa.

ANSWER.—One might ask whether this girl's condition is hereditary. If so, it will be difficult to help her. If her menstruation is normal there is evidence that her ovaries are secreting sufficient estrogenic hormone to develop the breasts. There are some women with small breasts who seemingly have normal glandular function. Because the breasts are small at present is no reason that they will not function normally if she should marry and become a mother. However, her present source of worry is the smallness of the breasts.

Since the girl's menstruation is normal, it is questionable whether estrogenic substance will help the condition, for she should be receiving a sufficient supply from her own ovaries, or menstruation would not be normal. If she is given the dosages of estrogenic substance mentioned, her menstrual cycle may be disturbed. If the breasts should develop under estrogenic stimulation there is no assurance that they will not revert to their original condition within thirty days after it is discontinued. The firmness and prominence of the breasts in a girl depend on the development of the gland trees and on the alveoli; massage will not develop these.

INJURY TO NERVES AT ELBOW

To the Editor:—After limited experience with nerve injuries in the upper extremity I wish to take exception to the answer to a question on this subject in The Journal, January 27, page 346. The picture so adequately described is typical of ulnar nerve paralysis without associated damage to the radial or median nerves. The muscles supplied by the ulnar nerve are the flexor carpi ulnaris, flexor digitorum profundus to the fourth and fifth fingers and all the intrinsic muscles of the hand except the abductor pollicis brevis, opponens pollicis, lateral head of the flexor pollicis brevis and the two lateral lumbricales (second and third fingers). In the case described the paralysis of two hours' duration may have been due to the immediate pain. The atrophy of the ulnar border and back of the hand is due to paralysis of the abductor, flexor brevis and opponens digiti quinti and of all the interossei respectively and is undoubtedly associated with atrophy of the palm as well. This explains the prominence of the bones and also the atrophy between the first and second metacarpals. The extension at the metacarpophalangeal joints and flexion at the interphalangeal joints, fourth and fifth fingers, without joint contracture, is due to paralysis of the medial two lumbricales which arise from the deep flexor and insert in the extensor tendons and which flex the proximal phalanx on the metacarpal and extend the middle and terminal phalanges. In the normal hand the action of the extensor communis digitorum on the metacarpophalangeal joints of the fourth and fifth fingers is opposed by the flexor profundus digitorium (medial half), the palmar and dorsal interossei and the lumbricales (medial half) supplied by the ulnar nerve and by the flexor sublimis digitorum supplied by the median nerve. In a lesion of the ulnar, therefore, the opposition of the extensor communis digitorum is reduced to only the flexor sublimis digitorum, which is not strong enough to supply the necessary antagonistic action, and the resulting unopposed action of the extensor communis digitorum results in hyperextension of the metacarpophalangeal joints of these digits. In an ulnar nerve lesion, extension of the interphalangeal joints of the fourth and fifth digits is feeble, because of the paralysis of the dorsal and palmar interossei and lumbricales affecting those digits. These intrinsic muscles are not only strong flexors of the metacarpophalangeal joints but by reason of their insertion into the aponeurosis of the extensor communis digitorum they are also extensors of the interphalangeal joints. This ability is well demonstrated in a complete lesion of the radial nerve, when the patient is able to extend the interphalangeal joints of the fingers completely. Severance of the radial nerve or extensor tendons is frequently undiagnosed because the interossei and part or all of the lumbricales are still intact and partial extension of the second to fifth fingers inclusive is still possible. Injury on the posterior aspect of the medial epicondyle could not readily cause damage to the median nerve, which passes anterior to the elbow or to the radial nerve, which passes anterior to the lateral condyle. If a roentgenogram has not been taken, one should be made of the elbows for comparison to determine whether the epicondyle was fractured and resulted in nonunion or malunion. I agree that the ulnar nerve should be explored and repaired and whether severed or intact it should be transplanted anterior to the epicondyle. If the epicondyle was fractured, the fragment should be removed. The radial nerve should not be explored unless there is other definite sensory or motor impairment.

Leonard T. Peterson, M.D., Washington, D. C.
Captain, M. C., U. S. Army.

VISUAL SCREENING TESTS AND VISION CHARTS

To the Editor:—Referring to the query of Dr. N. P. Andrews, Manitowoc, Wis., in The Journal, March 16, concerning visual screening tests and vision charts used in public schools with special reference to the Keystone telebinocular and Betts charts, we have been using the telebinocular in the Santa Monica, Calif., City Schools, of which I happen to be the Director of Health, for the past year and find it a very useful adjunct to our armamentarium. Our experience does not entirely coincide with the statements in the published answer to Dr. Andrews' query. The telebinocular is not used as a routine by the school nurses. We have an especially trained operator who uses it only in special cases that are referred to the office of the director. There is no attempt made to make any diagnosis whatever. The child either passes the tests to our satisfaction or the parents are advised by us that we believe the child needs further examination by an eye specialist. The statement that only three out of 100 children were able to pass these tests successfully does not coincide with our experience, as out of hundreds of children tested there have been comparatively few (less than 25 per cent) that we felt needed further examination. Our chief difficulty is in getting proper cooperation from nonmedical and so-called "cultist" eye specialists, who know nothing about the instrument. In practically every case in which we have made tests of children who have been seen by a competent ophthalmologist, our decisions have been corroborated that further testing was needed. We in the Health Department of the Santa Monica City Schools operate very closely in cooperation with the local branch of the Los Angeles County Medical Association.

Paul R. Burroughs, M.D., Santa Monica, Calif.
Director of Health.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, May 11, page 1952.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II, June 17-19. Part III, June or July, to be given in medical centers having five or more candidates desiring to take the examination. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: December 1940. *In view of the small number of applications received before March 1, there will be no examination at New York, June 10-14.* Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* October 21. Applications must be on file by September 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *General oral and pathologic examinations (Part II), (Group B)* will be conducted in Atlantic City, N. J., June 7-10. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* New York, June 8-10; Cleveland, Oct. 5. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF OTOLARYNGOLOGY: New York, June 3-5. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PATHOLOGY: New York, June 10-11. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: Memphis, Tenn., Nov. 17, preceding the annual meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF RADIOLOGY: New York, June 7-10. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., Rochester, Minn.

Pennsylvania January Report

Dr. James A. Newpher, director, State Board of Medical Education and Licensure, reports the examination held at Philadelphia, Jan. 2-6, 1940. Thirty-one candidates were examined, twenty-eight of whom passed and three failed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Universtiy of Arkansas School of Medicine		(1938)	1
Northwestern University Medical School		(1938)*	1
Louisiana State University School of Medicine		(1939)	1
University of Michigan Medical School		(1937)	1
Washington University School of Medicine		(1922)	1
Cornell University Medical College		(1938)	1
New York University College of Medicine		(1937)	1
University of Rochester School of Medicine		(1937)	1
Hahnemann Medical College and Hospital of Philadelphia		(1938),* (1938)	2
Jefferson Medical College of Philadelphia		(1937)	1
Temple University School of Medicine		(1938, 2)	2
University of Pennsylvania School of Medicine		(1937, 2), (1938)	3
Woman's Medical College of Pennsylvania		(1936), (1937)	2
McGill University Faculty of Medicine		(1938)*	1
Medizinische Fakultät der Universität, Wien		(1937, 2)	2
Deutsche Universität Medizinische Fakultät, Prag		(1922), (1937)	2
Université de Paris Faculté de Médecine		(1938)*	1
Friedrich-Alexanders-Universität Medizinische Fakultät, Erlangen		(1937)	1
Georg August-Universität Medizinische Fakultät, Göttingen		(1935)	1
Universiteit van Amsterdam Geneeskunde Faculteit		(1933)	1
Universität Bern Medizinische Fakultät		(1938)	1

School	FAILED	Year Grad.	Number Failed
Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest		(1915)	1
Regia Università degli Studi di Palermo. Facoltà di Medicina e Chirurgia		(1937)	1
Regia Università degli Studi di Messina. Facoltà di Medicina e Chirurgia		(1937	1

Five physicians were licensed by reciprocity and three physicians were licensed by endorsement from January 2 through January 19. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Maryland School of Medicine and College of Physicians and Surgeons		(1937)	Idaho
University of Michigan Medical School		(1933), (1936, 2)	Michigan
Hahnemann Medical College and Hospital of Philadelphia		(1938)	Maine

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Rush Medical College		(1924)	N. B. M. Ex.
Harvard Medical School		(1927)	N. B. M. Ex.
University of Michigan Medical School		(1932)	N. B. M. Ex.

* Licenses have not been issued.

Book Notices

A Text-Book of Occupational Diseases of the Skin. By Louis Schwartz, M.D., Medical Director, United States Public Health Service, in Charge of Dermatoses Investigations, Washington, D. C., and Louis Tulipan, M.D., Clinical Professor of Dermatology and Syphilology, New York University College of Medicine, New York City. Cloth. Price, $10. Pp. 799, with 116 illustrations. Philadelphia: Lea & Febiger, 1939.

The authors have devoted their careers to the subject of this work; hence they offer the most comprehensive volume thus far made available in this field. After a historical introduction, which indicates that Paracelsus was the first to write about occupational diseases, they take the reader to modern workmen's compensation laws. Next comes a consideration of the various causes of occupational dermatoses, diagnoses and some general considerations on methods of treatment. Succeeding chapters are devoted to innumerable industries and chemical substances, parasites and occupations associated with disturbances of the skin. Each chapter is followed by a comprehensive bibliography, and the illustrations are excellently chosen and well reproduced. The volume is a necessary item in the library of every dermatologist and worker in the field of industrial medicine.

Beyond the Clinical Frontiers: A Psychiatrist Views Crowd Behavior. By Edward A. Strecker, A.M., Sc.D., M.D., Professor of Psychiatry in the Undergraduate and Graduate Schools of Medicine, University of Pennsylvania, Philadelphia. Cloth. Price, $2. Pp. 210. New York: W. W. Norton & Company, Inc., 1940.

This volume presents the 1939 Salmon Memorial Lectures, the author being thus stamped as a leading psychiatrist. Dr. Strecker, as professor of psychiatry in the University of Pennsylvania, has established an enviable reputation as a sound, clear and progressive practitioner, thinker and writer. His approach to the problem is indicated by the subtitle, "A Psychiatrist Views Crowd Behavior"; that is, he takes psychiatry "beyond the clinical frontiers" and indicates how mental hygiene may develop defenses against the destructive behavior of the mob.

Just as the individual psychotic evades reality by withdrawal, rationalization, projection, aggression, repression, substitution and symbolization, so do we find similar mechanisms at work in various mob and "movement" activities. As symbolization is used by the psychotic for the purpose of psychic economy, so does the leader of the mob depend on the same principle. By means of the symbol exhibited before the mob, the annoyingly small i becomes the gloriously important, though unreal, WE. As the individual schizophrenic withdraws to his corner, so does the crowd engage in a "sit-down" strike. As the manic gives vent to his aggressiveness, so do nations go to war. And just as restraint provokes the manic to greater aggressiveness, so, perhaps, does the presence of armaments provoke to war.

What remedies may we expect? A more widespread and intensive application of mental hygiene principles in education—encouragement to face reality, a comprehension of the emotional motivation of conduct, recognition of the ominous power of the symbol, for instance. "There are not enough vistas which encourage thoughtfulness. First, the capacity to think, then a few quiet places in which to think, and finally some worthwhile things to think about—this would constitute the prescription of mental hygiene" (p. 182). And again (p. 197), "Environments will have to shift the frontiers of their realities. This is the equivalent of saying that individuals must be given better opportunities of acquiring, at least in elementary terms, self understanding and self development, and then they will be able to find self honesty. Once many individuals become capable of inner sincerity, then as collections of units they will constitute a society which will be honest with its members."

In this troubled world, where wars and rumors of wars daily insult our ears, this book should be read by every forward-looking citizen who has any hope (and most have!) that some time in the future we may develop a better formula by which man can live in peace and mutual respect with his fellow man. This book, by indicating in clear language some of the accepted facts as to the wellsprings of conduct, normal and abnormal, points the way.

Il lavoro nella chimica industriale. Dal Prof. Nicolò Castellino, direttore dell'Istituto di medicina del lavoro nella R. Università di Napoli. Paper. Price, 45 lire. Pp. 390, with illustrations. Milan: Ulrico Hoepli, 1940.

Professor Castellino, director of the Industrial Medicine Institute of the University of Naples, discusses twenty-five occupational diseases in the chemical industry and their causes. The diseases covered are those resulting from the use of acetone, aluminum, aniline, barium, benzene, berillium, cadmium, cobalt, fluorine, gallium, magnesium, molybdenum, nickel, carbon monoxide, tetra-ethyl lead, selenium, thallium, tellurium, carbon tetrachloride, titanium, thorium, trichlorethylene, tungsten and vanadium. This book does not assume that the diseases covered exhaust the exposures of the chemical industry. In truth, the number might have been extended threefold. The arrangement of topics is alphabetical so that the reader finds himself rapidly shifting from liquids to solids to gases, from hydrocarbon solvents to metals, with some resulting confusion. In many foreign books dealing with occupational diseases, frequently there is a dearth of references to publications of the United States. Some of the writers of this country are equally guilty or more so with regard to the publications of other countries. This book escapes that criticism, generously reviewing the record of investigations published in English. From the point of view of the American reader, the chief merit of the book is that it covers many metals little investigated in this country, such as gallium, cobalt, tungsten and vanadium. It can be commended to all Italian readers interested in occupational diseases. There is some temptation to suggest that a translation into English is warranted in order to make this helpful publication available to a much larger reading group.

Periodontal Diseases: Diagnosis and Treatment. By Arthur H. Merritt, D.D.S., M.S., F.A.C.D. Second edition. Cloth. Price, $3.50. Pp. 205, with 44 illustrations. New York: Macmillan Company, 1939.

In the preface the author points out that the purpose of his book is "to supply the needed information (as far as present knowledge permits) not only as it relates to periodontoclasia but in the entire field of periodontology. . . . It is intended to present the subject in as concise and simple a form as possible, since the busy practitioner is interested in its clinical rather than scientific aspect." The author has succeeded in presenting his material in such a concise and simple form that it should be easy reading for the "busy practitioner," but one is led to wonder, if the author had judiciously mixed more of the scientific with the clinical material, whether the same busy practitioner would not have had a better foundation on which to build a more rational and less empirical approach to the treatment of periodontal disease.

In the short chapter on classification of periodontal diseases we find grouped in four divisions gum recession, gingivitis, Vincent's infection and periodontoclasia. Under both gingivitis and periodontoclasia the author recognizes a systemic form. From a medical point of view it is to be regretted that more attention was not paid to these systemic forms, especially from an etiologic point of view, for such systemic disturbances as the deficiency diseases, the blood dyscrasias and some of the metabolic diseases such as diabetes, to mention only a few, result in secondary manifestations in the tissues supporting the teeth. These have always been given too little attention by both dentists and physicians. Perhaps one reason why scant attention was paid to this phase of the subject is the confidence the author has in the local technics of treatment, for he says in the chapter on systemic treatment "While, as has been said, it is desirable to have the cooperation of the physician in the treatment of cases of periodontoclasia, it is probably not done in most instances. And it may also be said for the encouragement of those general practitioners who make periodontia a part of their general practice and for the periodontists too that most cases get well and stay well by local treatment alone. When treatment as outlined in the preceding pages is skilfully done, one need not, as a rule, be greatly concerned about possible systemic treatment." Such statements as these are unfortunate, for while no one doubts the author's great technical skill it is difficult to see, for example, how local treatment in cases of a partial vitamin C deficiency producing oral symptoms, which are not at all rare, can bring about a permanent cure.

The prevention of these periodontal diseases is dealt with more briefly than its importance to both the dentist and the physician warrants. Certainly if advances are to be made in reducing the incidence of periodontoclasia, prevention looms large. There is no doubt, however, that the "practical dentist" looking for assistance in the technical methods of local treatment of the periodontal diseases will find it clearly presented in this book.

Tumors of the Hands and Feet. Edited by George T. Pack, B.S., M.D., F.A.C.S., Assistant Clinical Professor of Surgery, Yale University School of Medicine, New Haven. Cloth. Price, $3. Pp. 138, with illustrations. St. Louis: C. V. Mosby Company, 1939.

The large gilt letters on the back of this volume and the title page are somewhat deceptive, for unless one looked further one could easily fail to realize that the volume is a reprinting of a group of papers by eight authors which appeared originally in the January 1939 issue of *Surgery*. Dr. Pack has contributed the introduction and, with Dr. Frank Adair, a chapter on subungual melanoma, Dr. Michael L. Mason the chapter on carcinoma of the hands and feet, Drs. Ashley W. Oughterson and Robert Tennant the chapter on angiomatous tumors of the hands and feet, Dr. Alexander Brunschwig the chapter on tumors of the synovia, tendons and joint capsules of the hands and feet, and Drs. Bradley L. Coley and Norman L. Higinbotham the chapter on tumors primary in the bones of the hands and feet. The papers as a group are well written and well illustrated, though in several chapters (the introduction, the chapter on melanoma and the chapter on tumors of bone) photomicrographs are entirely lacking. Several fairly common types of tumor—large solitary lipoma, subfascial arborescent lipoma, neurofibroma, neurofibrosarcoma, epidermoid cysts of subcutaneous tissue and of bone are mentioned, if at all, only in a table indicating the distribution of tumors. Subungual melanoma and glomus tumors, already adequately described in surgical literature, are given a prominence hardly justified by their relatively infrequent occurrence.

Modern Society and Mental Disease. By Carney Landis, Ph.D., Associate Professor of Psychology, Columbia University, New York, and James D. Page, Ph.D., Instructor in Psychology, University of Rochester, Rochester, New York. Cloth. Price, $1.50. Pp. 190. New York: Farrar & Rinehart, Inc., 1938.

Among the many problems which especially confront the student of mental disease are the determination as to the effects of inheritance, the relative value to be assigned to environmental stress, such as war and economic depression, and finally the determination as to whether or not present methods of treatment, including hospitalization, are really effective. It is argued by some, for instance, that a rural life gives opportunity for introspection and brooding and by others that an urban life creates nervous tension. Where then is the person mentally afflicted to live?

The authors of this work classify mental diseases and provide us with excellent definitions of the effects of mental disturbances. They have traced the growth of the mentally diseased population, the figures indicating that around 600,000 people now inhabit our institutions for the mentally afflicted. The figures also show that at least one person out of every twenty will become a mental hospital patient at some time during his life. It becomes clear that, as with other diseases, the time when the patient comes under observation is of the utmost importance in the ultimate result.

One chapter on marriage and eugenics should answer the question as to whether or not married people have more trouble than those who are single and whether or not marriage of persons mentally afflicted is a eugenic threat. The authors are inclined to believe that these factors are, in general, not significant, although it is quite obvious that mental patients do not make ideal conjugal companions.

Other chapters concern heredity and sterilization and an analysis of mental disease in relation to population in this country as well as abroad. The conclusion is reached that the incidence of mental disease is increasing because more people are living longer. The book is supplemented by some valuable statistical tables. Among the most striking of the conclusions is the final paragraph, which emphasizes the fact that in mental disease particularly we must always bear in mind that the disease affects an individual.

Handbook of Skin Diseases. By Leon Hugh Warren, B.A., M.D., M.Sc., Acting Assistant Surgeon (Dermatology) in the Office of Dermatoses Investigations of the United States Public Health Service. With a foreword by Frederick D. Weidman, M.D. Fabrikoid. Price, $3.50. Pp. 321. New York & London: Paul B. Hoeber, Inc., 1940.

This book should be a useful adjunct to the dermatologist, particularly the dermatologist engaged in teaching. For it is, in effect, a collection of lecturers' notes brought down to date. It professes to be no more than a handbook, and the author has been faithful to his assignment. Forty-five pages are given to general principles of therapy. This section is especially well balanced, emphasizing the principles of therapy yet furnishing numerous workable prescription formulas, many of them with a thought to cosmetic properties. In the synopsis of skin diseases which makes up the remainder of the book, no attempt is made to adhere to any of the orthodox dermatologic classifications; rather the diseases are arranged in alphabetical order. Only their salient features are listed, both clinical and histopathologic; conditions to be differentiated are named, and a suitable line of treatment is outlined. Synonyms, eponyms and etymologic facts are given for each disease. There is a vast amount of material, with information that is current, and, to include it all in a small volume, the author has used a brief, often one word, telegraphic style. Inevitably it seems, errors creep into all books. Eczema, described as a protein disease, was probably meant to read a protean disease; and the paragraphs on dermatitis exfoliativa failed to mention the lymphoblastic type. As a handbook the volume is well done, especially the section on therapy. Because it is a handbook it will be of little value to the novice in dermatology. But for the teacher of dermatology, the practicing dermatologist and even for the student who will use it as a complement to his lecture notes or to a larger textbook, this little handbook should find a place.

Government and Economic Life: Development and Current Issues of American Public Policy. Volume I. By Leverett S. Lyon, Myron W. Watkins and Victor Abramson. Cloth. Price, $3. Pp. 519. Washington, D. C.: Brookings Institution, 1939.

This is one of the best contributions of the Brookings Institution. It provides an analysis of our economic life and its relation to the framework of our government. It then discusses relationships of government to private enterprise from the point of view of implementation and regulation. Chapters of especial interest at this time are, of course, those dealing with attempts to regulate monopoly and control competition. The volume provides vast numbers of references to the decisions of the courts with regard to attempts to adjust disputes between labor and industry and between various labor organizations and various industries. Somehow the philosophic consideration seems to fall short, however, in recognizing adequately the dual function of organizations of trades and industries for raising standards and benefiting the public, as well as the possibility that they may interfere with unlimited competition. Especially interesting also, in the light of modern activities, are those chapters of the work which take up the establishment of grading and standards in commerce. Here there is provided also a consideration of the new food and drug laws and the Wheeler-Lea act. Thus it is recognized that such standards must be established for the benefit of the public, but it seems to be urged that it is for the government alone to establish standards rather than to have these developed through voluntary agencies.

Sex and Life: Forty Years of Biological and Medical Experiments. By Eugen Steinach, M.D., Ph.D. The Scientific Values Adapted to the Lay Reader by Josef Loebel, M.D. Cloth. Price, $3.75. Pp. 252, with 67 illustrations. New York: Viking Press, 1940.

Apparently the publishers have been after Professor Steinach to write a popularization of his work. Succumbing to their solicitation, he provides a volume of promotional literature, fully illustrated with his photographs in many different aspects. It is his concept that sex rules life's shape and course. It is also his belief that his own investigations have been largely responsible for proving this concept, and the case reports published by some of his disciples who are in practice have not tended to mitigate in the slightest his belief. Thus for many years he and his disciples promoted the idea that the tying off of the vas would hold in the body the male and female sex hormones and would bring about a hypertrophy of the interstitial cells in which, they insisted, the sex hormones were elaborated. Fortunately it is now possible to secure these hormones in chemical form so that they may be injected into the body, which makes the surgical operation unnecessary.

When scientists develop these extraordinary concepts they are likely to forget many of the controls that are necessary in the evaluation of results. Thus Dr. Steinach has forgotten that surgical operation enhances the power of suggestion and that few human activities are more susceptible to psychologic suggestion than are those of a sexual character.

In his concluding chapter he promotes the idea that a mixture of female and male hormones lowers high blood pressure, but the evidence in this regard is not convincing.

An Introduction to Animal Biology. By John B. Parker, Ph.D., Professor of Biology, The Catholic University of America, Washington, D. C., and John J. Clarke, Ph.D., Assistant Professor of Biology, The Catholic University of America. Cloth. Price, $3.75. Pp. 503, with 163 illustrations. St. Louis: C. V. Mosby Company, 1939.

The authors have presented a carefully selected and orderly arranged mass of material. The aim to make the work "progressive, comparative and cumulative" has been kept in mind. The appendix and the glossary should prove of aid to the student who is beginning his study of the biologic sciences. Practical applications have been presented, as in the discussion of the relationship of insects to man and his activities and in the brief consideration of the pathogenic protozoa. The premedical student will find much in this textbook to stimulate his further interest in biology.

Nomenclature and Criteria for Diagnosis of Diseases of the Heart. By the Criteria Committee of the New York Heart Association. Fourth edition. Cloth. Pp. 282, with 52 illustrations. New York: New York Tuberculosis & Health Association, Inc., 1939.

This book deals first with the nomenclature and classification of heart disease and is supplemented by a section containing discussions of criteria for diagnosis, including the role of electrocardiograms and roentgenology. The book includes also an outline for the pathologic diagnosis of cardiovascular diseases and anomalies. The section on nomenclature follows in general that employed by the Standard Classified Nomenclature of Disease. The discussions on interpretation of roentgenograms of the heart and electrocardiograms are simple and constitute an invaluable guide to all clinicians dealing with heart disease. The book is well printed and the illustrations are clear. It should be in the hands of every cardiologist and internist and would prove useful to many others whose work with heart diseases is less specialized.

Infections of the Hand. By Lionel R. Fifield, F.R.C.S. Second edition by Patrick Clarkson, F.R.C.S., Surgical Tutor, Guy's Hospital, London. Cloth. Price, $3.25. Pp. 167, with 57 illustrations. New York: Paul B. Hoeber, Inc., 1939.

This is an admirable and concise presentation of the subject of infections of the hand and should be a helpful guide to students and practitioners. An excellent beginning chapter on the anatomy of the hand is followed by a chapter on prophylaxis of infections and by subsequent chapters—first on the simple infections, then on infections of the tendon sheaths, of the fascial spaces, on osteomyelitis, on lymphangitis and finally by a chapter on prognosis and on infections from the standpoint of workmen's compensation. Both the author and the editor of the new edition acknowledge their obligation to Kanavel and follow his teachings closely. They should be congratulated for the concise and excellent manner in which they have presented this important subject.

Reports on Medical Progress 1939 as Published in the New England Journal of Medicine. Compiled and Edited by Robert N. Nye, M.D. Cloth. Price, $5. Pp. 562. Boston: Little, Brown & Company, 1940

For many years the *New England Journal of Medicine* has been publishing reports of progress in various branches of medicine. Such a series was planned for the years 1938 through 1939 covering the specialties as well as general medicine and surgery. Each of the authors was asked to limit his statement to 4,000 words. Following each of the chapters there is a bibliography with references almost wholly limited to the years 1937 and 1938. Thus the reader who wishes to bring himself promptly abreast of current thought in a great many fields will find this a most useful volume. There is an excellent index.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Death from Pneumonia Following Reduction Under Ether of Fracture of Pelvis.—In the course of his employment as a miner, on Feb. 22, 1938, the workman was caught under a fall of slate. It took some forty-five minutes to remove him from the mine and carry him, wrapped in a blanket and on a stretcher, down a mountain through a cold rain to a physician. He was perspiring freely. The physician found him in shock and suffering intense pain from a fracture of his pelvis on the left side. After first aid treatment, the workman was taken in a closed automobile some 52 miles to a hospital. Physicians there found a "fracture of the left ilium extending down to the acetabulum" and determined that it would be necessary to reduce the fracture under ether, which was done two days later. February 27 pneumonia developed and the workman died March 4. The industrial commission of Virginia, in proceedings that were instituted under the workmen's compensation act of that state, found that pneumonia, the immediate cause of death, had not resulted naturally and unavoidably from the industrial accident and denied the workman's widow and children compensation. The claimants then appealed to the Supreme Court of Appeals of Virginia.

At the hearing before the industrial commission it appeared that the direct and immediate cause of death was acute lobar pneumonia. The five physicians who testified at that hearing agreed that this type of pneumonia is contagious and in a majority of cases is spread by "pneumococcus carriers," persons who themselves may or may not have had pneumonia but whose nasal and oral secretions for weeks and months contain virulent pneumococci. The evidence indicated that a week or more after visiting the workman in the hospital several friends and kinsmen contracted pneumonia. None of the physicians expressed an opinion as to the time or source from which the decedent contracted pneumonia, but they all agreed that it had developed to such an extent that its symptoms were apparent on February 27, the third day after the operation, and that the incubation period of the disease is usually from one to two days, sometimes longer. Each physician stated that the shock of fracturing his pelvis and the operation for reduction of the fracture so weakened the workman's general resistance as to make him "very susceptible to the development of the germ." The physicians further agreed that following the administration of ether there is always danger of pneumonia developing in the patient. On the basis of this testimony, the industrial commission found that the administration of ether to the workman had had nothing whatever to do with the pneumonia that subsequently developed, that the germ had already been present in the workman and that the pneumonia had developed coincidentally during the period of hospitalization for the fracture. The commission concluded, therefore, that the industrial accident had not been a producing cause of death.

The Supreme Court of Appeals of Virginia, however, disagreed with the conclusions of the industrial commission. The medical testimony just adverted to, said the court, when considered alone is vague, but when weighed with the conceded facts it strengthens rather than weakens the claimants' contention that the accident was the starting link in the chain of causation ending in death. There was no proof but merely a suggestion of possibility that the workman was a carrier of pneumococci. But, even if that suggestion be accepted as proof, the claimants are entitled to compensation if the accidental injury so influenced the progress of an existing disease as to cause death. An accident to an employee which sets in motion his undeveloped and dangerous physical condition with mortal consequences is properly classable as the proximate cause of the fatality. Causal connection is established when it is shown that an employee has received a compensable injury which materially aggravates or accelerates a preexisting latent disease which becomes the direct and immediate cause of death. The workman, continued the court, was hale and hearty for several years immediately preceding the accident. After the accident, exposure and operation he was confined to the hospital, where all proper precautions were taken to prevent the onslaught of pneumonia from any source. Notwithstanding these precautions, pneumonia developed in an otherwise apparently vigorous and healthy man within five days from the date of the accident and within three days from the date that ether was administered, resulting in death some five days later. In the absence of positive affirmative evidence, tending to establish a break in the chain of causation, the inevitable conclusion from the evidence is that the death of the workman resulted naturally and unavoidably from the accident.

Accordingly, the court reversed the order of the industrial commission and remanded the case to it with directions to allow the claimants the amount of compensation permitted by law.—*Justice v. Panther Coal Co., Inc. (Va.), 2 S. E. (2d) 333.*

Workmen's Compensation Acts: Liability of Employer for Noncompensable Occupational Disease.—Two suits, one a common law action for negligence and the other an action under a wrongful death statute, were brought against respective employers of two workmen who, in the course of their employment as sandblasters and operators of grinding machines, contracted silicosis or pneumoconiosis sometime prior to 1937. It was alleged that the employers had been negligent in that, contrary to the duties imposed on them by common law, by safety statutes and by rules of the industrial commission, they failed to furnish a safe place to work, failed to disclose to employees the dangerous conditions of their employment and failed to provide proper safety and protective devices. The workmen's compensation act of Ohio, in effect at the time the employees contracted their disabilities, provided compensation for only those occupational diseases enumerated in a schedule. As silicosis was not at that time included in that schedule, it was not compensable. This occupational disease, however, was later included in the schedule by an amendment to the compensation act in 1937. The defendant employers demurred to the complaints and in effect contended that no cause of action was maintainable at common law or under the wrongful death statute because such right, if any ever existed, had been taken away by the workmen's compensation act and by constitutional provisions relating to workmen's compensation. After judgments of two courts of appeals affirming judgments of the trial courts sustaining the demurrers, the two cases were consolidated and appealed to the Supreme Court of Ohio.

There was never a time, said the Supreme Court, when an action could not be maintained for an occupational disease provided all the elements were present which gave the employee a right of action for negligence according to the principles of the common law. For instance, if an employer is guilty of negligence in failing to maintain safe working conditions, and such negligence is the proximate cause of an occupational disease, the employee can bring an action for damages for the employer's negligence. In those states in which all or a part of the occupational diseases have not been made compensable under workmen's compensation acts, the overwhelming weight of authority is that the employee has a right of action at common law for negligence of the employer proximately causing a noncompensable occupational disease. Also, the safety statutes of Ohio which require the employer to furnish a safe place to work and to furnish and use proper safety devices and the rules of the industrial commission relative to the prevention of silicosis or pneumoconiosis impose duties on the employer which, on violation by the employer proximately resulting in the employee contracting an occupational disease, enable the employee to maintain an action for damages against the employer.

At the time workmen's compensation was first adopted in Ohio, said the court, an action for an occupational disease or for wrongful death therefrom could be maintained against an employer guilty of actionable negligence. From a study of the workmen's compensation act and the provisions of the Ohio constitution relating to workmen's compensation, the court could find no provision which abolished the right of an employee to

bring an action for damages for an occupational disease, not compensable under the workmen's compensation act, contracted as the result of the employer's negligence. Since the underlying purpose of compensation is to make industry bear the burden of human wreckage by paying stated awards for injury and loss of life in the course of employment, the court believed it should avoid any strained constitutional or statutory construction relative to workmen's compensation which would leave many employees, who were blameless victims of their employers' torts, without either damages or compensation and absolutely remediless. It would be an obvious injustice to allow compensation to some employees who contract occupational diseases and allow others nothing, not even damages, for occupational diseases tortiously inflicted.

Accordingly, the Supreme Court reversed the judgments in favor of the defendant employers and remanded the causes of action to the trial courts for further proceedings on the merits. —*Triff v. National Bronze & Aluminum Foundry Co.; Smith v. Lau (Ohio), 20 N. E. (2d) 232.*

Workmen's Compensation Acts: Liability of Physician for Malpractice in Treatment of Industrial Injury.—In the course of her employment in a laundry the plaintiff sustained an injury to her spine, consisting of fractures of one or more vertebrae. By a settlement with her employer she obtained an award of compensation for $1,500 under the workmen's compensation act of Illinois. Subsequently she brought suit for malpractice against the defendant physician whom she had engaged to treat her. She alleged that she had suffered injury because the physician had neglected to examine her and diagnose her condition, to perform an operation on her spine which she claimed was indicated and to reset the fractured vertebrae. Among other things, the defendant physician contended that the injury which the plaintiff alleged she received at his hands was but an aggravation of an injury which she had received in the course of her employment and so the settlement of compensation released him from liability for damages. From a judgment of the appellate court, second district, reversing a judgment of the trial court in her favor, the plaintiff appealed to the Supreme Court of Illinois.

The workmen's compensation act of Illinois provides that, where an employee's compensable injury or death was not proximately caused by the negligence of the employer or his employees but was caused under circumstances creating a legal liability on the part of some person other than the employer to pay damages, legal proceedings may be brought against such third person, if he has elected not to be bound by the act, to recover damages notwithstanding the employer's payment of or liability to pay compensation under the act. The act further provides that, if in the legal proceedings against such third person a judgment is obtained and paid or a settlement is made, from the amount received by the injured employee or his personal representative there shall be paid to the employer the amount of compensation paid or to be paid by the employer to such employee or personal representative. The defendant physician contended that he was not a third party within the meaning of these provisions of the act because he did not inflict the injury but only aggravated an injury which the employer had already caused. With this contention the court could not agree because to so construe these provisions would be to defeat their purpose, which is to require indemnification of the employer, where he is compelled to pay compensation as a direct result of the negligence of a third person, out of money recovered by the injured employee from such negligent third person. While an employer is liable for aggravation, due to malpractice, of an employee's injury, he is also liable for injury caused entirely by third persons through no fault of his own. In the instant case the employer had to pay an amount of money, in addition to compensation for the original injury, to cover the aggravation, caused by the defendant's malpractice, of the employee's injury. To adopt defendant's contention, said the court, would deprive the employer of his right of subrogation and confer on defendant a benefit to which he was in no way entitled.

Accordingly, the Supreme Court held that the appellate court correctly decided that the payment of compensation under the workmen's compensation act was not a valid defense available to the defendant physician. However, because the appellate court had erred in holding that the suit had been barred by the statute of limitations, the judgment of the appellate court was reversed and that of the trial court in favor of the plaintiff affirmed.—*Huntoon v. Pritchard (Ill.), 20 N. E. (2d) 53.*

Society Proceedings

COMING MEETINGS

American Medical Association, New York, June 10-14. Dr. Olin West, 535 N. Dearborn St., Chicago, Secretary.

American Association for the Surgery of Trauma, Atlantic City, N. J., June 7-8. Dr. Ralph G. Carothers, 409 Broadway, Cincinnati, Secretary.

American Association for Thoracic Surgery, Cleveland, June 6-8. Dr. Richard H. Meade Jr., 2116 Pine St., Philadelphia, Secretary.

American Association of Genito-Urinary Surgeons, Skytop, Pa., June 20-22. Dr. Charles C. Higgins, 2020 East 93d St., Cleveland, Secretary.

American Association on Mental Deficiency, Atlantic City, N. J., May 22-26. Dr. E. Arthur Whitney, Washington Road, Elwyn, Pa., Secretary.

American Broncho-Esophagological Association, New York, June 5. Dr. Paul Holinger, 1150 N. State St., Chicago, Secretary.

American College of Chest Physicians, New York, June 8-10. Dr. Robert B. Homan Jr., P. O. Box 1069, El Paso, Texas, Secretary.

American College of Radiology, New York, June 12. Mr. M. F. Cahal, 540 North Michigan Bvld., Chicago, Executive Secretary.

American Gastro-Enterological Association, Atlantic City, N. J., June 10-11. Dr. Albert F. R. Andresen, 88 Sixth Ave., Brooklyn, N. Y., Secretary.

American Gynecological Society, Quebec, Canada, June 17-19. Dr. Richard W. TeLinde, 11 East Chase St., Baltimore, Secretary.

American Heart Association, New York, June 7-8. Dr. Howard B. Sprague, 50 West 50th St., New York, Secretary.

American Laryngological Association, Rye, N. Y., May 27-29. Dr. C. J. Imperatori, 108 East 38th St., New York, Secretary.

American Laryngological, Rhinological and Otological Society, New York, June 6-8. Dr. C. Stewart Nash, 277 Alexander St., Rochester, N. Y., Secretary.

American Medical Women's Association, New York, June 9-10. Dr. Elizabeth Parker, 1835 Eye St., Washington, D. C., Secretary.

American Neurological Association, Rye, N. Y., June 5-7. Dr. Henry A. Riley, 117 East 72d St., New York, Secretary.

American Ophthalmological Society, Hot Springs, Va., June 3-5. Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn., Secretary.

American Otological Society, Rye, N. Y., May 30-31. Dr. Isidore Friesner, 36 East 73d St., New York, Secretary Pro-Tem.

American Physiotherapy Association, New York, June 23-28. Mrs. Eloise T. Landis, 2065 Adelbert Rd., Cleveland, Secretary.

American Proctologic Society, Richmond, Va., June 9-11. Dr. Curtice Rosser, 710 Medical Arts Bldg., Dallas, Texas, Secretary.

American Psychiatric Association, Cincinnati, May 20-24. Dr. Arthur H. Ruggles, 305 Blackstone Blvd., Providence, R. I., Secretary.

American Radium Society, New York, June 10-11. Dr. William E. Costolow, 1407 South Hope St., Los Angeles, Secretary.

American Rheumatism Association, New York, June 10. Dr. Loring T. Swaim, 372 Marlborough St., Boston, Secretary.

American Society of Clinical Pathologists, New York, June 6-10. Dr. Alfred S. Giordano, 531 N. Main St., South Bend, Ind., Secretary.

American Therapeutic Society, New York, June 7-8. Dr. Oscar B. Hunter, 1835 Eye St. N.W., Washington, D. C., Secretary.

American Urological Association, Buffalo, N. Y., June 24-27. Dr. Clyde L. Deming, 789 Howard Ave., New Haven, Conn., Secretary.

Association for the Study of Internal Secretions, New York, June 10-11. Dr. E. Kost Shelton, 921 Westwood Blvd., Los Angeles, Secretary.

Connecticut State Medical Society, Hartford, May 22-23. Dr. Creighton Barker, 258 Church St., New Haven, Secretary.

Illinois State Medical Society, Peoria, May 21-23. Dr. Harold M. Camp, 224 South Main St., Monmouth, Secretary.

Maine Medical Association, Rangeley Lakes, June 23-25. Dr. F. R. Carter, 22 Arsenal St., Portland, Secretary.

Massachusetts Medical Society, Boston, May 21-22. Dr. Alexander S. Begg, 8 Fenway, Boston, Secretary.

Medical Library Association, Portland, Ore., June 25-27. Miss Anna C. Holt, 25 Shattuck St., Boston, Secretary.

Montana, Medical Association of, Bozeman, June 18-20. Dr. Thomas F. Walker, 206 Medical Arts Building, Great Falls, Secretary.

National Gastroenterological Association, New York, June 4-6. Dr. G. Randolph Manning, Room 319, 1819 Broadway, New York, Secretary.

National Tuberculosis Association, Cleveland, June 3-6. Dr. Charles J. Hatfield, 50 West 50th St., New York, Secretary.

New Jersey, Medical Society of, Atlantic City, June 4-6. Dr. Alfred Stahl, 55 Lincoln Park, Newark, Secretary.

New Mexico Medical Society, Albuquerque, May 27-29. Dr. L. B. Cohenour, 219 West Central Ave., Albuquerque, Secretary.

New York State Association of Public Health Laboratories, Rochester, May 20. Miss Mary B. Kirkbride, New Scotland Ave., Albany, Secretary.

Pacific Northwest Medical Association, Spokane, Wash., June 26-29. Dr. C. W. Countryman, 407 Riverside Ave., Spokane, Wash., Secretary.

Rhode Island Medical Society, Providence, June 5-6. Dr. Guy W. Wells, 124 Waterman St., Providence, Secretary.

Society of Surgeons of New Jersey, Paterson, May 22. Dr. Walter B. Mount, 21 Plymouth St., Montclair, Secretary.

South Dakota State Medical Association, Watertown, May 20-22. Dr. Clarence E. Sherwood, Madison, Secretary.

Texas, State Medical Association of, Dallas, May 13-16. Dr. Holman Taylor, 1404 West El Paso St., Fort Worth, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia

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Renal Lesion in Obstructive Jaundice. L. L. Thompson Jr., W. D. Frazier and I. S. Ravdin, Philadelphia.—p. 305.

Tuberculosis of Nasopharynx: Positive Sputum with Roentgenographically Negative Chest. J. W. Trenis, Ann Arbor, Mich.—p. 312.

Hemorrhagic Diathesis with Prolonged Coagulation Time Associated with Circulating Anticoagulant. E. L. Lozner, L. S. Jolliffe and F. H. L. Taylor, Boston.—p. 318.

Trichinosis: Study of Twenty-Three Cases. F. D. Murphy, Harriet D. James and J. W. Rastetter, Milwaukee.—p. 328.

Studies with Agar Cup-Plate Method: II. Effect of Blood on Mercury Antiseptics. S. B. Rose and Ruth E. Miller, Philadelphia.—p. 338.

*New Diagnostic Test (Galactose) for Thyroid Disease. T. L. Althausen, J. C. Lockhart and M. H. Soley, San Francisco.—p. 342.

Pharmacologic and Pathologic Effects of Repeated Convulsant Doses of Metrazol. R. W. Whitehead, K. T. Neubürger, Enid K. Rutledge and W. L. Silcott, Denver.—p. 352.

Pressor Action of Benzedrine and Paredrine. A. Iglauer and M. D. Altschule, Boston.—p. 359.

*Effect of Sulfapyridine Alone and with Serum on Pneumococcic Pneumonia and on Pneumococcus-Infected Marrow Cultures. J. G. M. Bullowa, New York; E. E. Osgood, Portland, Ore.; S. C. Bukantz, New York, and Inez E. Brownlee, Portland, Ore.—p. 364.

Fatal Case of Hemolytic Anemia and Nephrotic Uremia Following Sulfapyridine Administration. J. M. Ravid and C. Chesner, Brooklyn.—p. 380.

Parenteral Administration of Sulfapyridine. J. W. Haviland, Baltimore, and F. G. Blake, New Haven, Conn.—p. 385.

*Observations on Pharmacology and Toxicology of Sulfathiazole in Man. J. G. Reinhold, H. F. Flippin and L. Schwartz, Philadelphia.—p. 393.

Galactose Test for Thyroid Disease.—Althausen and his associates report on the galactose tolerance test applied in 130 cases of hyperthyroidism, 121 in which hyperthyroidism was absent and seven cases of myxedema. The test consists of the oral administration of galactose followed by determinations of blood galactose thirty minutes and sixty minutes later. From the distribution of the peaks of the galactose curves in subjects with and without hyperthyroidism the normal range for the maximal concentration of galactose in the blood under conditions of the test was between 10 and 30 mg. per hundred cubic centimeters. A peak between 30 and 40 mg. lies in the doubtful range. Values exceeding 40 mg. and below 10 mg. are abnormal. The test was positive in 124 cases, doubtful in five and negative in one of the 130 cases of hyperthyroidism. Of eighty-seven cases presenting conditions other than hyperthyroidism, proved hepatic insufficiency or Paget's disease the test was positive in seven, doubtful in ten and negative in seventy. In four of the seven cases in which the test was positive, hepatic involvement was suspected. The galactose tolerance curve was abnormally low in six of the seven cases of myxedema, and barely within the lower limit of normal in one. In the normal state, little if any galactose is found in five minute specimens. In hyperthyroidism, increased intestinal absorption of sugars is expressed not only by a high peak of the galactose curve but also, in about one half of the cases, by a premature appearance in the blood of considerable amounts of galactose. Therefore the finding of 10 mg. per hundred cubic centimeters or more of galactose in five minute specimens is an additional criterion in favor of the diagnosis of hyperthyroidism. This criterion is most useful in instances in which the peak of the galactose curve is in the doubtful zone. A comparison of the galactose test with the basal metabolic rates of the hyperthyroid patients showed no close quantitative correlation, although usually patients with extremely high basal metabolic rates also had equally high values for galactose. Probably the best explanation for lack of correlation is that elevation of the basal metabolic rate and stimulation of absorption are relatively independent effects of thyroxine which occur to varying degree in different patients. In comparing the value of the galactose test with that of the basal metabolic rate, it appears that among patients with definite clinical hyperthyroidism doubtful results are encountered somewhat less frequently with the galactose test. This is probably due to the fact that the intestinal absorption of sugars is more sensitive to the influence of a small excess of circulating thyroxine than is the basal metabolism. When the basal metabolic rate is found to be elevated in patients with hyperthyroidism, that test seems to offer a more accurate index of the degree of hyperthyroidism than does the galactose tolerance test. In the differential diagnosis of hyperthyroidism, the galactose test is useful in cases of low grade hyperthyroidism, especially when the basal metabolic rate is less than plus 20, and in patients without hyperthyroidism who have an abnormally elevated basal metabolic rate. Fifteen of the 130 patients with hyperthyroidism belong in the first classification, and in all of these the galactose test was positive. In the second classification were eight patients suffering from anxiety states with hyperventilation and four patients with obscure cardiac dyspnea. The basal metabolic rate of these twelve patients ranged from plus 22 to 36, whereas the galactose test was negative in ten cases and doubtful in two. In five patients with nontoxic adenoma of the thyroid or with Hashimoto's struma, the results of the galactose tolerance test corresponded to estimations of the basal metabolic rate. Advanced hepatic insufficiency and Paget's disease interfere with the use of the test for the diagnosis of hyperthyroidism. Intravenous administration of galactose to patients with hyperthyroidism showed that, as a rule, utilization of galactose in this condition is normal. Usually subtotal thyroidectomy promptly restores the blood galactose curve to normal.

Effect of Sulfapyridine and Serum on Pneumococci.—The technic of vaccine vial culture of human marrow, permitting controlled quantitative studies of the interaction of living cells, bacteria and therapeutic agents, is extended by Bullowa and his associates to include sulfapyridine in an attempt to evaluate the importance of adding specific serum in the treatment of pneumonia. Their observations indicate that serum plus sulfapyridine is a more effective therapeutic agent than either acting alone in the early cases when autogenous antibody cannot be expected to be present. It was suggested recently that serum plus sulfapyridine may be essential when the severity of a pneumococcic infection is so great that capsular polysaccharide is detected in the blood. The authors' studies indicated that pneumococci may remain viable for as long as fifty-four hours, despite the presence of sulfapyridine and serum, and that large inoculums may undergo temporary bacteriostasis with subsequent overgrowth. Summarizing their experimental studies the authors state that: 1. In marrow cultures the presence of sulfapyridine in concentrations of 5 mg. or more per hundred cubic centimeters may lead to ultimate sterility with inoculums of 500 or less cubic centimeters of types I, III or VII pneumococci, whereas controls uniformly grow out to more than 100 million colonies per hundred cubic centimeters. 2. The larger the initial inoculation, the less likely is sulfapyridine to lead to sterility. 3. Sulfapyridine alone is definitely more effective against pneumococci than equimolar concentrations of sulfanilamide. 4. The presence of type specific antiserum almost always increases the effectiveness of sulfapyridine. With the same concentrations of sulfapyridine, increasing quantities of antibodies are increasingly effective. Occasionally the presence of serum interferes with the bactericidal action of sulfapyridine in vitro. 5. Within the range of concentrations employed, varying from 1 to 10,000 to 1 to 100,000, an increase in concentration of sulfapyridine results in an increase in effectiveness. 6. Different strains of pneumococci appear to vary in their susceptibility to sulfanilamide and sulfapyridine. Freshly isolated virulent strains appear to be less susceptible than strains that have been grown in ordinary mediums. 7. The presence of sulfapyridine does not result in rapid death of all organisms present. Small numbers of living organisms may be present for several days in cultures which appear microscopically sterile. 8. Sulfapyridine, in the concentrations employed, has not appeared to damage directly the marrow cells or to favor or inhibit phagocytosis. 9. Organisms exposed to the action of sulfapyridine undergo no loss of capsule or type specificity. They may, however, become dis-

torted, develop long chains and stain irregularly. 10. Acetylsulfapyridine is ineffective. 11. Serum from untreated pneumonia patients is not bactericidal. The serum from treated patients has bactericidal activity roughly proportional to its content of sulfapyridine and serum. 12. Sulfapyridine alone gave a lower death rate than either serum alone or serum plus sulfapyridine, in a series of 324 adult patients rotated for treatment. The lowest mortality rate was observed in cases treated early (from one to four days) with serum and sulfapyridine.

Pharmacology and Toxicology of Sulfathiazole.—Reinhold and his co-workers discuss the pharmacologic and toxic effects of sulfathiazole on human beings. They conducted two groups of experiments: those in which a single dose of the drug was administered orally, intravenously or rectally and those in which multiple doses were administered for several days. Its effects were observed in nine convalescent patients serving as controls and in eighty-three patients suffering from pneumonia. It was found that sulfathiazole is rapidly absorbed from the gastrointestinal tract and is rapidly excreted in the urine. Following intravenous administration of the sodium salt, recovery of sulfathiazole in the urine is practically quantitative. It is not readily absorbed from the rectum. The proportion of the drug conjugated is low in most individuals. Effects observed on renal function and the hemopoietic system were transitory and not pronounced. Vomiting occurred in about 10 per cent but was never severe enough to interfere with the use of the drug. The incidence of other toxic reactions was small. Because sulfathiazole is absorbed more readily from the gastrointestinal tract and is excreted more rapidly than sulfapyridine, its use therapeutically is more easily controlled, an advantage that at times may be of decided importance.

American Journal of Physiology, Baltimore

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Accuracy of Plate Counts Made from Milk Products as Affected by Temperature of Incubation. C. S. Pederson and R. S. Breed, Geneva, N. Y.—p. 162.

Newer Medical Methods of Appraisal of Nutritional Status. W. Schmidt, New York.—p. 165.

Importance of Economical Milk in Human Nutrition. Marietta Eichelberger, Chicago.—p. 169.

Chemical Agents in Prevention and Treatment of Experimental Poliomyelitis. E. W. Schultz, Stanford University, Calif.—p. 175.

Studies of the Kahn Test: I. Special Tube for Preparation of Antigen Suspension. M. B. Kurtz and E. M. Hill, Lansing, Mich.—p. 180.

Recent Investigations of Goat's Milk. A. K. Besley, Beltsville, Md.—p. 182.

American Journal of Surgery, New York

47:553-746 (March) 1940

Peripheral Nerve Injuries, with Results of Early and Delayed Suture. C. R. G. Forrester, Chicago.—p. 555.

*Pathologic Factors Found in Surgical Investigation of Epilepsy. K. W. Ney, New York.—p. 573.

Relation of Certain Seminal Findings to Fertility, with Special Reference to Sperm Concentration and Significance of Testicular Epithelial Cells in Semen. G. L. Moench, New York.—p. 586.

*Combined Intra-Uterine, Extra-Uterine Pregnancy: Review of 291 Cases in Literature and Report of Three New Cases. A. Bernstein, San Francisco.—p. 597.

Acute Abdomen, with Special Reference to Symptoms, Diagnosis and Surgical Treatment. A. M. Vaughn, Chicago.—p. 602.

Peptic Ulcer of Meckel's Diverticulum: Case Report and Review of Literature. J. G. Matt and P. J. Timpone, New York.—p. 612.

Ptosis of Cecum and Ascending Colon. A. C. Silverberg, Seattle.—p. 624.

Mesenteric Vascular Disease. J. E. Dunphy and R. D. Whitfield, Boston.—p. 632.

Interposition of Vitallium Plates in Arthroplasties of Knee: Preliminary Report. W. C. Campbell, Memphis, Tenn.—p. 639.

Discogenetic Disease. A. Oppenheimer, Beirut, Lebanon, Syria.—p. 642.

Pathologic Changes in Epilepsy.—In a series of 272 patients with the "idiopathic" type of epilepsy Ney has found almost invariably definite lesions at operation. In 225, corticodural fixations at the cerebral vertex in or near the cortical motor areas were localized roentgenologically with the aid of subdural air insufflation. Arachnoidal defects or fistulas through which cerebrospinal fluid leaks into the subdural space have been found in practically every epileptic patient operated on. These fistulas are probably the result of tears in the arachnoid which have failed to heal. They are usually located at the extreme vertex of the brain, where the strain of gravity is greatest. During subdural air insufflation it is possible to demonstrate that cerebral postural stability is dependent on the maintenance of arachnoidodural approximation. This approximation is controlled by fluid film adhesion between the arachnoid and the dura, which maintains these structures in forceful apposition and a negative subdural pressure which develops when fluid film adhesion is lost through an excess of subdural fluid. This subdural negative pressure maintains the brain in a certain degree of postural stability but tends to siphon cerebrospinal fluid into the subdural space through arachnoidal fistulas when these are present. The traction on the cortex which occurs in expansive lesions and corticodural adhesions after craniocerebral trauma seems to be a factor responsible for the induction of convulsive phenomena in these two diverse pathologic conditions. During operation, traction serves to induce attacks. In the "idiopathic" type of epilepsy definite traction is exerted on corticodural attachments at the extreme vertex of the brain during postural displacement, which occurs when there is an excess of subdural fluid. Subdural air insufflation aids in the localization of corticodural attachments. It shows the cerebral postural displacement which takes place when air or excessive fluid enters the subdural space. The fluid level changes with the position of the head. The surgical correction of arachnoidal fistulas and the reduction of traction on corticodural attachments have so diminished convulsive attacks in his patients that the author feels justified in considering the lesions described as causative factors in chronic convulsive states.

Combined Intra-Uterine and Extra-Uterine Pregnancy.—Bernstein considers only those cases in which extra-uterine and intra-uterine pregnancies were concurrent and simultaneous. An analysis of 276 cases collected by Novak in 1926, and of fifteen cases reported since and three of his own, reveals that the mortality in the entire series was 20.7 per cent, or 14.4 per cent if cases are excluded in which the condition was discovered only post mortem. These patients did not receive treatment. The maximal incidence of such pregnancies was in the active period of childbirth, from 26 to 35 years of age, with a tendency to fall in the latter half of the period. The previous parity suggests that previous labors predispose to the condition. The two pregnancies may occur at the same time or the uterine conception may antedate the extra-uterine, and vice versa. A normal pregnancy may occur while the dead products of an ectopic gestation are still present. The period of pregnancy varied from eleven weeks to term. The cause of nine deaths was internal hemorrhage. Symptoms were present from a few hours to the whole duration of pregnancy. Forty-one instances, with six deaths, were discovered after labor had started. Half

of these patients presented no symptoms except an unusual increase in the size of the abdomen. The intra-uterine pregnancy of six patients was terminated by abortion. In half of the patients after delivery a symptomless mass was observed in the abdomen. The other half had varying symptoms usually suggestive of infection or intestinal irritation. The symptoms of twelve patients were so insignificant that nothing was done for the palpable mass. Eight fetuses were passed piecemeal through fistulas, with death of one mother. A live child was removed from the abdomen on five occasions from one to twenty-three days after labor began. Sixteen patients had exploratory laparotomies and two died. The cause of death of three other women was peritonitis and intraperitoneal hemorrhage of one. The condition of twenty patients was diagnosed in the second half of pregnancy or during labor. All were operated on and seven died from hemorrhage, septicemia, pulmonary embolism or pulmonary edema. Two deaths occurred in the sixth month, one in the seventh and four at term.

Archives of Ophthalmology, Chicago

23:477-688 (March) 1940

Analysis of Operative Results in Concomitant Convergent Strabismus. G. G. Gibson, Philadelphia.—p. 477.
Medical Treatment of Senile Cataract. A. C. Krause, Chicago.—p. 487.
Bilateral Symmetric Cystoid Detachment of Retina. A. L. Kornzweig, New York.—p. 491.
Necroscleritis Nodosa Associated with Chronic Rheumatoid Polyarthritis: Report of Case. H. Eggers, New York.—p. 501.
*Place of Coats's Disease Among Diseases of Retina. H. Elwyn, New York.—p. 507.
Plastic Repair of Conjunctival Defects with Fetal Membranes. A. de Rötth, Spokane, Wash.—p. 522.
Santa Lucia, Patroness of the Eyes. E. M. Blake, New Haven, Conn.—p. 526.
Bilateral Uveitis Associated with Detachment of Retina (Harada's Disease). A. Rados, Newark, N. J.—p. 534.
Relation of Dynamic to Static Refraction in Presbyopic Patients 40 Through 50 Years of Age. H. F. Sudranski, Indianapolis.—p. 545.
New Corneoscleral Suture. J. M. McLean, Baltimore.—p. 554.
The Orthoptic Technician as an Aid to the Ophthalmologist. Julia E. Lancaster, San Francisco.—p. 560.
*Lindau's Disease: Report of Six Cases, with Surgical Verification in Four Living Patients. A. E. MacDonald, Toronto.—p. 564.
Syndrome of Neuromyelitis Optica. J. L. Fetterman and W. P. Chamberlain Jr., Cleveland.—p. 577.
Vaccinia with Ocular Involvement. W. S. Atkinson and G. Scullard, Watertown, N. Y.—p. 584.
Experimental Retinoblastoma. A. Weil and L. L. Mayer, Chicago.—p. 591.
Glioma of Optic Nerve: Critical Review: Report of Two Cases, with Autopsy Observations in One. J. M. Wilson and W. D. Farmer, Durham, N. C.—p. 605.
Orthoptics at the Crossroads. E. Krimsky, Brooklyn.—p. 619.

Coats's Disease of the Retina.—Elwyn believes that the exudate and the connective tissue formation in the retina in Coats's disease are the consequences of local circulatory disturbances, beginning with transudations of plasma and of blood. The transudations and hemorrhages are the immediate results of peristasis and prestasis and of rupture of small abnormal and dilated vessels. The small abnormal vessels represent a congenital malformation involving branches of the central retinal vessels. These vascular malformations find their proper place in a classification of vascular malformations and tumors of the cerebral circulation. The disease occurs mostly in young persons and usually affects only one eye. It progresses slowly and is unnoticed until vision is greatly diminished or completely lost or a divergent strabismus occurs. The cornea, anterior chamber, iris and lens are normal in the early stages; the vitreous may show opacities. Characteristic of the disease is the occurrence of single or multiple white or yellowish white exudates in the fundus. The exudate at times is gray or greenish. It is situated mainly behind the retinal vessels. Hemorrhages in the retina occur in practically every case, near the veins, on the crest of the exudate or in its periphery. Glistening points and deposits of cholesterol are seen frequently. Deposits of pigment occasionally occur. The disk is usually normal and may be slightly hyperemic. Changes in the retinal vessels are mainly in the small vessels peripheral to the secondary and the tertiary branches, affect the veins more than the arteries and are limited to one retinal area. They consist of fusiform and spherical dilatations, loops, twists and tortuosities. The end result is partial or total blindness complicated by cataract formation, iritis, glaucoma or softening of the globe.

Lindau's Disease.—MacDonald encountered six cases of Lindau's disease among eleven members in two generations of two families. Of the remaining five only one was examined and his vision was found defective. The sight of the other four was said to be normal. In three cases the diagnosis of Lindau's disease has been verified by craniotomy, and in a fourth case, that of a blind sister of one of the three patients, a cerebellar hemangio-endothelioma was removed. All four patients have since returned to their work. The mother of two of the patients of the first family died after an operation for tumor of the brain. The father of two of the patients in the other family died of intracranial complications. Both of these parents had been blind in one eye for five years before death. The surgical diagnosis of two of the living patients has been confirmed by pathologic examination. Prior to 1928 fatal results were uniformly reported in the treatment of Lindau's disease. The condition is usually seen in the second or the third decade of life. The year 1928 may mark the division of Lindau's disease into fatal and nonfatal, as the widespread complications reported by the early writers will no longer be seen. The cerebellar tumors of Lindau's disease are found in about one out of every five patients who suffer from retinal angiomatosis or Hippel's disease. The three cases in the author's second family may be considered as belonging to a group in which diagnosis is yet to be confirmed. There is no record in the fourth case of a retinal angioma, and the cerebellar angioma was lost at operation, when the small mural tumor disappeared in the sucker as the surrounding cyst was evacuated. The failure to diagnose the condition as Lindau's disease in one of these cases until after operation leads the author to believe that blindness without a history of trauma, when associated with the factor of heredity, should be considered as a possible equivalent of retinal angiomatosis. The essential cause of blindness in the first case of the first family was obscure until the operation on the second patient for hemangio-endothelioma, and even then confirmation was difficult by pathologic examination owing to the small size of the retinal tumor. The successful treatment of retinal angiomatosis by radon seeds has been recorded by Foster Moore. In treating the second patient four 0.7 millicurie radon seeds were used. They were attached to a silk suture at intervals of about 4 mm. for seven days on the sclera opposite the tumor. Removal of the seeds was facilitated by dipping them and the silk sutures in liquid pyroxylin before insertion. The terms Hippel's disease and Lindau's disease must be retained, for, while both conditions have a familial tendency, Hippel's disease may occur without complications. Multiple hemangio-endotheliomas must be demonstrated to justify diagnosis of Lindau's disease and, if only one tumor is found, familial incidence must be shown.

Arkansas Medical Society Journal, Fort Smith

36:221-240 (March) 1940

Treatment of Antepartum Hemorrhage. B. J. Reaves, Little Rock.—p. 221.
Aciform Treatment of Rheumatic Disorders. F. J. Scully, Hot Springs National Park.—p. 225.

Florida Medical Association Journal, Jacksonville

26:373-424 (Feb.) 1940

Acute Appendicitis. L. J. Netto, West Palm Beach.—p. 383.
Acute Intestinal Obstruction: Diagnosis and Physiologic Treatment. H. West, DeLand.—p. 387.
Yellow Jack. G. N. MacDonell, Miami.—p. 391.
Coronary Occlusion in General Practice. T. C. Kenaston, Cocoa.—p. 394.
Clinical Endocrinology of the Male, with Especial Reference to Male Climacteric. C. P. Lamar, Miami.—p. 398.

Journal of Aviation Medicine, St. Paul

11:1-56 (March) 1940

Forum on Air Line Medical Problems. H. B. Wright, Cleveland.—p. 2.
*Syndrome of Vasomotor Instability as Seen in Examinations of Cadet Applicants for Flying. C. L. Leedham, Randolph Field, Texas.—p. 20.
Some Observations on Aviation Cadet Selection. W. W. Davies.—p. 37.

Vasomotor Instability in Applicants for Flying.—Leedham determined the incidence of vasomotor instability in 679 applicants for appointment as flying cadets in the United States Army. Of these, 202 were accepted unqualifiedly as physically fit, twenty-three were disqualified on remediable defects and 454 were rejected. The cardiovascular system contributed either

wholly or in part to 178 rejections. In thirty-five the cardiovascular system was the only disqualifying factor, while vasomotor instability played a part in 138 rejections. The author considers vasomotor instability to be a minor degree of neurocirculatory asthenia. The diagnostic points of vasomotor instability as interpreted at the School of Aviation Medicine are a low Schneider index, unstable blood pressure, unstable pulse rate and a coarse tremor. To these may be added symptoms and signs of neurocirculatory asthenia. The cause of vasomotor instability in the applicants has not been elucidated. The group studied consisted of healthy men between 20 and 27, preselected by the educational requirement of two years of college work. Hence the author believes that they should have been the cream of the population. It is possible that the condition is an incident to better breeding, the mental capacity and stress required for the successful completion of two years of college work. There has been no work of a control nature to prove or disprove this hypothesis. The author's study indicates that this syndrome is not a physical condition. There is no significant trend except possibly in the weight, especially the underweight, which suggests that individuals chronically underweight, whether from asthenic build or from some other undiscovered constitutional factor, have a greater incidence of vasomotor instability. He believes that vasomotor instability is a neurogenic entity, probably a part of a generalized emotional instability. The condition does not depend on a disease of the vasomotor apparatus but is an expression of instability or lack of normal control, apparently by the vasomotor centers. The condition is present in adults who are apparently in good physical condition. Many of these individuals passed every other portion of the examination for flying but were found to be unstable and easily excited.

Kansas Medical Society Journal, Topeka

41:89-132 (March) 1940

Coronary Sclerosis. C. A. Hellwig, Wichita.—p. 89.
Xanthoma Tuberosum: Report of Case. M. Delp, Kansas City.—p. 95.
Observations on Eyes During Metrazol Treatment. L. S. Powell, Lawrence; M. E. Hyde and J. Russell, Osawatomie.—p. 97.

Medical Annals of District of Columbia, Washington

9:71-108 (March) 1940

Methods for Measurement of Pressures in Antecubital and Popliteal Veins During Exercise. J. R. Veal and H. H. Hussey, Washington.—p. 71.
Traction Manipulation Treatment of "Stiff Neck." J. S. Neviaser, Washington.—p. 75.
Treatment of Staphylococcic Septicemia with Sulfamethylthiazole: Report of Case with Recovery. T. F. Keliher and S. A. Carlen, Washington.—p. 78.
Treatment of Pneumococcic Peritonitis with Sulfamido Drugs and Serum: Report of Two Cases. W. W. Sager, Washington.—p. 81.
Sulfapyridine: Is It a Safe Drug? T. G. Klumpp and R. W. Weilerstein, Washington.—p. 83.

Michigan State Medical Society Journal, Lansing

39:157-228 (March) 1940

*Chronic Cholecystitis: Present Medical and Surgical Status. W. H. Cole, Chicago.—p. 173.
Occupational Dermatoses: Treatment and Prevention. L. Schwartz, Washington, D. C.—p. 179.
*Control of Pneumonia. L. D. Felton, Washington, D. C.—p. 181.
Posterolateral Dislocation of Elbow: Associated with Displacement of Internal Epicondyle into Joint. D. Somers and A. Goetz, Detroit.—p. 188.
Bacillary Dysentery. V. L. Barker, Monroe.—p. 190.
Headache and Head Pain of Ocular Origin. A. D. Ruedemann, Cleveland.—p. 191.
Sterility: Recent Trends in Its Investigation and Treatment. C. P. Huber, Indianapolis.—p. 193.

Chronic Cholecystitis.—Cole asserts that relief of gallstone obstruction of the common duct accompanying chronic cholecystitis represents the one condition in which an urgent operation is indicated. Other indications are dependent on the amount of pain and the prevention of complications. The latter consideration is of importance, as death from gallbladder disease results from complications of the disease and not from the lesion itself. At least half of the patients with disease of the gallbladder are without symptoms. At present there is a tendency to ignore these instances of "silent gallbladder," except that the presence of stones in a young person may be sufficient cause for cholecystectomy. The author believes that in general there is far too much conservatism displayed in the operative treatment of aged people with disease of the gallbladder, particularly since the aged succumb readily to the complications of cholecystitis. It is not fully appreciated that aged people tolerate abdominal operations including cholecystectomy quite well provided they have no serious complicating disease, but they do not tolerate the complications of cholecystitis. New developments in anesthesia eliminate to a great extent the previous serious danger of postoperative pneumonia in the aged. The diagnosis of disease of the gallbladder should be definite before operation is advised. Failure to obtain relief is often due to the performance of operation with the wrong diagnosis. Cholecystitis is so common that in many instances a second disease will be present and it will be causing the symptoms. If acute pancreatitis is present, operation is strongly indicated even though the symptoms of cholecystitis may be mild. Operation for attacks of cholecystitis during pregnancy is rarely indicated because symptoms frequently disappear after parturition. Results following cholecystectomy are generally much better in the group of patients complaining of severe pain in the right upper quadrant which radiates posteriorly, while results will be poor in the group complaining of dyspepsia with only mild pain. Biliary dyskinesia accounts for a portion of the failures following cholecystectomy. The type and thoroughness of the operation often determine the result; an ill advised cholecystostomy may be followed by recurrence of symptoms which would have been relieved completely by cholecystectomy. Cholecystectomy itself does not shorten life. In general, complicating diseases not secondary to the cholecystitis are contraindications to operation, whereas diseases secondary to gallbladder disease increase the indication for operation unless they have progressed to the point at which operability is seriously jeopardized.

Control of Pneumonia.—Felton cites Gundel to the effect that pneumococci were not found in the respiratory passages of newborn infants but might occur on the second or third day. He found pneumococci in 60 per cent of 100 infants. He concluded that vegetative forms of pneumococci were not instrumental in causing pneumonia but believed that the causative organism came from without. A higher percentage of pneumonia results from contact with an actual case; but if this were the sole source it would be difficult to explain many isolated cases of pneumonia and the origin of the pneumococci capable of producing disease. Man harbors pneumococci with greater frequency than any other animal and with a greater diversity of pneumococcus types. He either furnishes the soil for the different varieties of this bacteriologic seed or produces variants of a common variety depending on biochemical differences in individual animals. The pneumococcus varies in invasive power or virulence with the different seasons of the year. The observation that incidence of pneumonia is higher in contacts than in carriers indicates an acquired virulence by passage through man. The commensal relationship of the pneumococcus and man cannot be overlooked. Evidently the organism maintains sufficient disease-producing characteristics to allow invasion when conditions of the host will permit. The greater the virulence of the organism, the greater is its invasiveness; but the greater the virulence, the greater is its antigenicity. If the host is capable of responding to the antigen supplied by the pneumococcus with the formation of antibodies, the barrier against invasion is increased and the organism becomes avirulent. The virulent organism carries with it the ability to produce disease or to produce immunity of the host. The specific antibody is probably not the only defense of the host. The natural resistance may be the most important method in the control of infectious disease. More than 25 per cent of the general population harbor the pneumococcus. This percentage probably represents those persons who respond well to pneumococcus antigen and are highly resistant to infection. The explanation as to why one individual out of 500 contracts lobar pneumonia annually might well be related to the ability of the host to respond to the antigen present in the commensal parasite. Serum titrations, both before and after immunization with type I pneumococcus, of 641 individuals from 2 to 79 years of age show, contrary to expectations, that there apparently is no difference in antibody response in the various decades. The serums from 70.6 per cent of the individuals before immunization failed to show demonstrable protective antibodies. After immunization only 5.9 per cent were negative. The same

general result was found in the case of the type II pneumococcus. The problem is to determine whether or not persons who fail to respond and those who respond poorly are highly susceptible to pneumococcic infection or lobar pneumonia, and those who respond well are resistant. Preliminary study of the antibody content shows that there is no relationship between serum antibody titer and intensity of reaction. Efforts must be made toward analysis of the conditions which change the normal commensal to a virulent parasite. The methods of controlling pneumonia are the cure of the disease and its prevention by increasing the resistance of the host nonspecifically or specifically. Definite advances in its cure have been made during the last fifteen years. Serum therapy decreased the mortality of lobar pneumonia for the first time in the history of medicine.

Military Surgeon, Washington, D. C.

86:225-340 (March) 1940

Effect of Cold on Oxygen Content of Blood: Preliminary Report. M. C. Grow.—p. 225.
*Prophylactic Treatment of Wounds in War. P. M. Keating and F. M. Davis.—p. 235.
Eighteen Years of Pneumonia at William Beaumont General Hospital El Paso, Texas. T. E. Scott and E. M. Nielsen.—p. 241.
Calcium Metabolism and Teeth: Summary of Present Day Knowledge. R. Kronfeld.—p. 250.
Marching Efficiency. A. Steindler.—p. 256.
Horace Wells, The Man—The Benefactor. P. W. Brown, F. R. Krug and R. D. Darby.—p. 263.
Aneurysms of Aorta. D. C. Collins.—p. 270.
Practical Method of Localizing a Foreign Body in the Eye, When a Sweet's Localizer Is Not Available. J. M. Love.—p. 281.
Contusion of Kidney. D. B. Stearns.—p. 284.
Foot Strain, Simple Method of Treatment. L. Cozen.—p. 290.
Insulin and Metrazol Treatment of Psychoses. J. M. Nielson.—p. 298.

Prophylactic Treatment of War Wounds.—The primary requisite of military surgery, according to Keating and Davis, is to send the wounded back to duty as quickly as possible and with the least possible mutilation. Treatment differs from its civilian prototype mostly in that it usually cannot be instituted quickly because of evacuating difficulties. Experience during the last two years has shown that prophylactic roentgen treatment in industrial cases of penetrating, perforating and crushing wounds, given a few hours after their reception, perceptibly decreases the percentage of infections by gas forming organisms, as well as by streptococci and staphylococci. These industrial wounds are closely comparable to those received in combat. This prophylactic treatment of dirty wounds, in addition to the accepted cleansing and débridement, makes primary closure a frequent success and is frequently successful even if fractures are plated immediately. To make this type of treatment available to soldiers it will be necessary to install adequate x-ray apparatus at the first well equipped surgical establishment through which the wounded are passed and operated on during their evacuation to the rear. It is suggested that these prophylactic x-ray units be placed in the mobile surgical hospitals.

New England Journal of Medicine, Boston

222:373-424 (March 7) 1940

*Combined Degeneration of Spinal Cord in Pernicious Anemia: Results of Seven Years' Experience with Parenteral Liver Therapy. M. B. Strauss, P. Solomon and H. J. Fox, Boston.—p. 373.
*Regional Ileitis. S. F. Marshall, Boston.—p. 375.
Neurosurgery. D. Munro, Boston.—p. 308.

Degeneration of Spinal Cord in Pernicious Anemia.—Strauss and his associates reported in THE JOURNAL, May 4, 1935, on the efficacy of parenteral liver therapy for the neural manifestations of pernicious anemia. Spinal cord lesions of uncomplicated pernicious anemia could be completely arrested by adequate parenterally administered liver extract. Patients without neural lesions did not develop spinal cord degeneration when adequately treated. These conclusions were based on a study of twenty-six patients with marked spinal cord lesions and eighty patients with minimal or no neural lesions, treated for an average period of three years. Twenty-one of the first group and sixty-four of the second were observed for an additional four years, making a total of eighty-five patients observed for an average period of seven years. In none of the twenty-one cases of marked involvement of the spinal cord did any objective neurologic sign become more marked during the seven year period of treatment nor did an abnormal sign, not previously present, appear. This indicates a complete arrest of the degenerative process. The sixty-four patients had either no signs referable to the nervous system or else evidence of mild lesions not interfering with their ability to walk. In none of these has any further evidence of neural damage appeared. This indicates that adequate therapy prevents the development of degeneration of the spinal cord in pernicious anemia. Adequate treatment demands that enough extract must be given to maintain the blood values at normal. Not only should the red cells number 4,500,000 or higher, but the mean corpuscular volume should be below 100 cubic microns, and the color index 1 or below. There must be no glossitis or indigestion. Recurrence of numbness, tingling or other paresthesia of the extremities calls for increase in the dose of liver extract. If the patient presents other subjective manifestations that might be attributed to progression of the spinal cord lesions, the dose should be doubled.

Regional Ileitis.—Marshall reports forty-eight cases of regional ileitis observed at the Lahey Clinic during the last six years. Operations were performed in twenty-nine of these. Involvement of the ileocecal junction was noted in sixteen. The cause of the disease has not been established. The work by Felsen suggests a dysentery bacillus as the causative agent, but such bacilli have not been isolated from the resected specimens. The condition was also believed to be due to lymphatic disease of the mesentery, with the production of marked lymphedema of the bowel wall. Association between regional ileitis and lymphadenitis of early childhood caused by small unrecognized lesions of the mucosa is a possibility. It is a disease of young adults, occurring most commonly in the third and fourth decades. The symptoms are pain in the right lower quadrant, nausea, diarrhea, loss of weight and anemia. The course of the disease is that of a chronic, progressive inflammatory process, which may persist for months or years. The onset may be acute with symptoms resembling those of acute appendicitis. Of the twenty-nine patients operated on, fifteen had had a previous appendectomy, the true nature of the disease apparently being recognized only twice. Symptoms of intestinal obstruction are not uncommon, though a complete obstruction rarely occurs. One of the commonest complications is the occurrence of fistulas, which may be either internal or external. The diagnosis is established by x-ray examination. Characteristic filling defects are noted in the terminal ileum. In the advanced cases marked stenosis of the bowel reduces the lumen so that only a thin, irregular linear shadow is seen, presenting the "string sign" of Kantor. The filling defects of the terminal ileum just proximal to the cecum are characteristic. The x-ray observations in conjunction with the history establish the diagnosis in the majority of cases. At the Lahey Clinic resection of the terminal ileum, cecum and ascending colon by the Mikulicz technic was practiced. To attempt such an extensive resection with immediate primary anastomosis greatly increases the operative hazard and is unjustifiable in view of the excellent results and the comparative safety with which a two stage Mikulicz type of resection can be carried out in a large majority of cases. Recurrences are probably associated with incomplete removal of the affected bowel, and for this reason the author advocates wide excision of the affected loop. He believes that the cecum should be removed in all cases in which the terminal ileum is involved.

New Orleans Medical and Surgical Journal

92:489-544 (March) 1940

Aims of Appendicitis Committee of Surgical Section of Southern Medical Association. I. Cohn, New Orleans.—p. 489.
Diagnosis of Acute Appendicitis. H. R. Kahle, New Orleans.—p. 490.
Management of the Patient with Possible Appendicitis. S. Karlin, New Orleans.—p. 494.
Age Factors in Acute Appendicitis. C. J. Miangolarra, New Orleans.—p. 496.
Mistakes Commonly Made in Treatment of Syphilis of Nervous System. C. S. Holbrook, New Orleans.—p. 498.
Cor Pulmonale. B. R. Heninger, New Orleans.—p. 506.
Treatment of Trichomonas Vaginalis Vaginitis with Sodium Perborate: Preliminary Report of Fourteen Cases. E. C. Smith, New Orleans.—p. 510.
Endometrial Changes and Their Relation to Ovarian Dysfunction. J. R. Kriz and H. J. Schattenberg, New Orleans.—p. 514.
Fractures of Upper End of Humerus Treated by Early Relaxed Motion and Massage. R. H. Alldredge and M. P. Knight, New Orleans.—p. 519.

North Carolina Medical Journal, Winston-Salem

1:125-176 (March) 1940

Medical Research: The Story of Sulfanilamide. E. K. Marshall Jr., Baltimore.—p. 125.
Urgent Surgery on Infants Under One Year of Age. F. W. Griffith, Asheville.—p. 129.
Prevention and Treatment of Pelvic Floor Injuries. B. P. Watson, New York.—p. 134.
Tuberculosis Case Finding Program in a Woman's College. Ruth M. Collings, Greensboro.—p. 138.
Chronic Acetanilid Poisoning with Addiction. D. McIntosh Jr., Marion. —p. 143.
Management of Old Contractures of Hand Resulting from Third Degree Burns. R. Jones Jr., Durham.—p. 148.
Diagnosis and Treatment of Neurosyphilis. J. P. Davis, Winston-Salem. —p. 152.
Analysis of Deaths Among Individuals with Syphilis in North Carolina During 1938: Preliminary Report. G. M. Leiby, Washington, D. C. —p. 156.
Artificial Rupturing of Membranes as Method of Induction of Labor. J. C. Taylor, Washington, N. C.—p. 159.

Public Health Reports, Washington, D. C.

55:303-346 (Feb. 23) 1940

Further Study of Mode of Action of Methylcholanthrene on Normal Tissue Cultures. W. R. Earle and C. Voegtlin.—p. 303.
Our Verbal Public Health Activities. J. W. Mountin.—p. 323.

55:347-386 (March 1) 1940

Study of Pneumococcus Typing Serums for Purpose of Standardizing a Test for Potency. Bernice E. Eddy.—p. 347.
Yellow Fever. J. H. Bauer.—p. 362.
Notes on Variation in Eggs of Anopheles Punctipennis Say. W. K. Lawlor.—p. 371.

55:387-440 (March 8) 1940

Place of an Index in Health Department Record Keeping. J. W. Mountin and Evelyn Flook.—p. 387.
Studies of Sewage Purification: XI. Removal of Glucose from Substrates by Activated Sludge. C. C. Ruchhoft, J. F. Kachmar and W. A. Moore.—p. 393.

Rhode Island Medical Journal, Providence

23:31-46 (March) 1940

Providence Medical Association. H. C. Messinger, Providence.—p. 31.
Sulfanilamide Therapy at Rhode Island Hospital. R. O. Bowman, Providence.—p. 33.

Surgery, Gynecology and Obstetrics, Chicago

70:603-730 (March) 1940. **Partial Index**

Fetal Swallowing, Gastrointestinal Activity and Defecation in Amnio: Experimental Roentgenologic Study in Guinea Pig. R. F. Becker, W. F. Windle, E. E. Barth and M. D. Schulz, Chicago.—p. 603.
Malignant Changes in Fibro-Adenoma of Mammary Gland. S. W. Harrington and J. M. Miller, Rochester, Minn.—p. 615.
Management of Breech Delivery. T. R. Goethals, Boston.—p. 620.
Anoxia and Oxygen Therapy in Head Injury. J. G. Schnedorf, R. A. Munslow, A. S. Crawford and R. D. McClure, Detroit.—p. 628.
*Consideration of So-Called "Granulosa" and "Theca" Cell Tumors of Ovary. H. F. Traut and A. A. Marchetti, New York.—p. 632.
Anatomy of Subperitoneal Tissues and Ligamentous Structures in Relation to Surgery of Female Pelvic Viscera. A. H. Curtis, B. J. Anson and L. E. Beaton, Chicago.—p. 643.
Anesthesia in Cesarean Section. K. M. Heard, Toronto.—p. 657.
The Problem for Surgery in Treatment of Massive Hemorrhage of Ulcer Origin. C. S. Welch and A. M. Yunich, Albany, N. Y.—p. 662.
Significance of Nutrition and Gastric Acidity in Etiology of Experimental Peptic Ulcer. A. Slive, W. H. Bachrach and S. J. Fogelson, Chicago. —p. 666.
*Relation of Chronic Cystic Mastitis to Malignancy. I. M. Procter, Raleigh, N. C.; C. C. Carpenter and R. P. Morehead, Wake Forest, N. C.—p. 671.
Operations for Gallstones. V. M. Coppleson, Sydney, Australia.—p. 679.
New Plan of Antecolic Duodenojejunal Anastomosis. F. H. Lahey, Boston.—p. 689.
Repair of Defects of Frontal Bone. G. B. New and C. R. Dix, Rochester, Minn.—p. 698.

"Granulosa" and "Theca" Cell Tumors of Ovary.—Traut and Marchetti present the criteria and the differentiation of the two main types of cells of theca and granulosa cell tumors. They arrive at differentiation of the theca and granulosa cells on the basis of their studies with the Foot silver stain. Neoplastic granulosa cells occur in islands consisting of from a few to several hundred cells. They seldom exist singly. The islands are surrounded by strands or networks of reticulum containing numerous theca cells and the vascular supply. The nuclei of theca and granulosa cells are impossible to distinguish from one another, as they contain similar nucleolar and chromatin bodies. However, the cytoplasm of the granulosa cell contains many argentophil granules, whereas the cytoplasm of the theca cell is almost devoid of these bodies. The theca cell is always in intimate relationship with the reticular framework to such a degree that each cell is surrounded by a capsule of this material which isolates it from the neighboring theca cells. The granulosa cells are seen in groups, usually of large numbers, each cell being in immediate contact with its neighboring granulosa cells. The island of granulosa cells is surrounded but not penetrated by the reticulum. The application of these differential points affords a new approach to the study of this group of tumors, which will yield data not formerly obtainable. In attempting to outline the life cycle of these tumors and its relationship to the clinical syndrome, the authors point out that most graafian follicle tumors produce symptoms which bring the patient to the physician, with the result that the great majority of them are removed before they have reached the end of their life cycle. It is therefore necessary to postulate some of the terminal aspects of the neoplasms. If the tumor is not adversely affected by such accidents as ischemia or hematoma formation, the cells tend to mature and to undergo quite typical degenerative changes. The theca cells reach the end of their life cycle sooner than do the granulosa cells. Luteinization occurs in both types and this is followed by collagenous degeneration, which is replaced by fibrosis. The greater the content of theca cells, the more likely is the tumor to produce fibrous connective tissue. The granulosa elements, however, being poorly supplied with supporting framework on which to dispose themselves and being less intimately supplied with blood vessels, are more prone to premature accidents which interrupt the other forms of degeneration that might otherwise ensue.

Chronic Cystic Mastitis and Malignancy.—Procter and his co-workers point out that the breast is constantly undergoing periodic changes of progression and regression (hyperplasia and involution) from birth to senility. The histologic picture is changed weekly if not daily. The breast is under the direct control of the ovary, and the ovary is under the control of the anterior pituitary. The ovary exerts a dual hormonal influence on the breast, the periacinous and periductal connective tissue being governed by the follicular and interstitial elements of the ovary, while the duct and acinous epithelium is under the control of the corpus luteum. If this control becomes abnormal by a disturbance in the time or volume of hormone liberation, the periodic mammary changes may cross the borderline from the physiologic into a pathologic state. The breast is continuously undergoing changes of progression and regression as a result of hormone stimulation. As the endocrine life of the individual is different during the various decades, pathologic change will bear a close relationship to these decades. During the first decade of menstrual life two common pathologic changes occur: periductal and intracanalicular fibro-adenomas. These are probably the result of excessive hormone stimulation or endocrine hypersensitivity on the part of certain tissues. During the second decade the borderline between the physiologic and pathologic is frequently crossed and "chronic cystic mastitis" develops. The various changes that take place are probably the result of ovarian stimulation. In contrast to the first decade, the epithelium is involved instead of the connective tissue. This altered physiology results in the production of chronic cystic mastitis and the blue dome cyst of Bloodgood. If adenosis (Cheatle and Cutler) is the predominating feature, microscopic examination of the area reveals epithelial proliferation with the formation of small intracystic papillomas or nonencapsulated adenomatous areas. The cystic disease may be characterized by the formation of one or several well developed cysts. Bloodgood contended that these lesions had no relationship to malignant growth. However, if the entire gland is sectioned dilated ducts containing intraductal papillomas are frequently observed and these not infrequently show the presence of malignant alteration. In the third decade of menstrual life certain breasts fail to cease activity with cystic hyperplasia and go on to benign neoplasia and possibly to carcinoma. The active epithelium is laid down layer by layer to form sessile papillomas. In other instances connective tissue stalks invade the epithelial growths and true papillomas are formed. At times the multiple papillomas attach themselves one to the other to form new gland surfaces and

adenomatous masses, so-called comedo adenomas of Bloodgood. The authors' series of cases have proved to their satisfaction the existence of both benign intraductal adenomas and various degrees of malignant change in duct carcinoma. In cases microscopically malignant, they obtained both success and failure following complete operation and high voltage roentgen therapy. Cutler has shown cyst papilloma and carcinoma in the same duct and has set forth evidence that 20 per cent of all carcinomas of the breast originate in cystigerous desquamative epithelial hyperplasia. The evidence at hand seems to favor the idea that the greater number of pathologic changes in the breast are of hormone origin. Experimental investigation has established the dependence of mammary connective tissue development on the follicular hormone and of epithelial tissue activity on the corpus luteum. If the relationship between ovarian secretion and mammary activity is accepted it is easy to visualize a disturbance in this delicate balance with resulting disturbances in hyperplasia and involution. In many cases the fault may lie with the anterior pituitary, as this gland is the dynamic motor activator of the ovary. The patient rarely calls attention to induration and fine nodularity of the breast but is greatly concerned, and properly so, when a solitary mass appears. When the latter occurs, hormone treatment should never be instituted. The authors prepare such patients for radical operation and remove the tumor, excising a wide margin of normal breast tissue. Immediate frozen sections are made and if the lesion is benign the wound is closed; if malignant, the radical operation is performed at once and is followed by adequate high voltage roentgen therapy. The authors feel that the obstetrician should instruct patients about the care of the breast as well as of the uterus and that the gynecologist and surgeon should work together with the pathologist in the operating room and laboratory in order to reach a more accurate diagnosis and most efficient treatment.

Texas State Journal of Medicine, Fort Worth

35:745-816 (March) 1940

The Prostate: Medical and Surgical Aspects. H. H. Young, Baltimore.—p. 751.
Diagnosis of Intestinal Obstruction. S. E. Russ, San Antonio.—p. 754.
Acute Intestinal Obstruction. J. V. Goode, Dallas.—p. 756.
Regional Enteritis. L. W. Baird, Temple.—p. 760.
Colitis. T. Miller, Dallas.—p. 764.
Generalized Cryptococcosis Simulating Hodgkin's Disease. May Owen, Fort Worth.—p. 767.
Urinary Complications of Carcinoma of Cervix. J. O. Chambers, Galveston.—p. 771.
Treatment of Cancer of Skin by X-Rays. H. Klapproth, Sherman.—p. 776.
Sulfanilamide in Ophthalmology. C. S. Sykes, Galveston.—p. 780.
Vascularization of Cornea. W. E. Muldoon, San Antonio.—p. 783.
Infectious Diseases of Animals Transmissible to Man That Are Prevalent in Texas. T. O. Booth, Fort Worth.—p. 787.
The Health Officer's Responsibility in the Dental Health Program. E. Taylor, Austin.—p. 793.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

48:129-204 (March) 1940

Rupture of Kidney. A. H. Peacock, Seattle.—p. 129.
Clinical Significance of Neurofibromatosis (von Recklinghausen's Disease). D. Trueblood, Seattle.—p. 134.
Essential Principles in Treatment of Tetanus. D. R. Jensen, New York.—p. 146.
Rhabdomyosarcoma and Other Myocardial Tumors: Report of Three Cases. C. P. Larson, Tacoma, Wash., and W. L. Lidbeck, Salem, Ore.—p. 151.
Endometriosis: Clinical Review. H. von Geldern, San Francisco.—p. 154.
Formation of Artificial Vagina. E. P. Steinmetz, Portland, Ore.—p. 169.
Ectopic Pregnancy. H. N. Shaw, Los Angeles.—p. 181.

Wisconsin Medical Journal, Madison

39:153-252 (March) 1940

Early Diagnosis of Cancer in General Practice. M. Fernan-Nunez, Milwaukee.—p. 169.
Comments on Pollen Therapy, with Special Reference to Its Application in Wisconsin. H. J. Lee, Oshkosh.—p. 175.
Significant Details in Routine Health Examination of Children: Examination of the Eye, Ear, Nose, Throat and Orthopedic and General Considerations. F. H. Haessler, Milwaukee; J. E. Mulsow, Milwaukee; L. A. Copps, Marshfield; W. P. Blount and R. M. Greenthal, Milwaukee.—p. 179.
Transvaginal X-Ray Treatment of Cervical Cancer. A. W. Erskine, Cedar Rapids, Iowa.—p. 184.
Otolaryngologic Aspects of Blood Dyscrasias. W. E. Grove, Milwaukee.—p. 188.
Surgical Treatment of Prostatic Obstruction. J. B. Wear, Madison.—p. 192.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

1:377-424 (March 9) 1940

*Preparation and Use of Dried Plasma for Transfusion. F. R. Edwards, J. Kay and T. B. Davie.—p. 377.
Treatment and Primary Suture of Face Wounds. E. D. D. Davis.—p. 381.
Two Commonly Misunderstood Skin Conditions in Infancy. I. Gordon.—p. 383.
Stitch for Use in the Harris Prostatectomy. O. S. Hillman.—p. 385.
Postpartum Retinal Arterial Obstruction Associated with Hemiplegia. A. M. W. Thomson.—p. 387.

Dried Plasma for Transfusion.—Edwards and his co-workers point out that the formation of blood banks has made available a considerable supply of plasma. It is the plasma protein element of a blood transfusion that produces the desired effect; the erythrocytes play a secondary part. Plasma will keep indefinitely as compared with stored blood and no grouping of the recipient is necessary. Blood may be taken from donors for the purpose of obtaining plasma, in which case the stored blood should be kept undisturbed for a period of from three to four days to allow the maximal separation of plasma from the erythrocytes. Most of the plasma the authors used has been obtained from bottles of citrated stored blood about fourteen days old. If these bottles have not been disturbed since the erythrocytes have settled, practically clear plasma can be withdrawn without any disturbance of the layers in contact with the erythrocytes. A slight discoloration by hemoglobin is of no disadvantage and its administration seems to be innocuous. Although administration of pure plasma has been satisfactory, if the plasma could be dried, storage and transportability would be greatly simplified and the possibility of bacterial growth greatly reduced. The authors devised a continuous-feed plasma drier. The plasma is suctioned over in a thin stream into a special container and there dried. It is removed later under aseptic conditions and stored in ampules. About 8 Gm. of the dried product is obtained from 100 cc. of citrated plasma. The dried plasma is dissolved in the ratio of 8 Gm. to 100 cc. of warm distilled water; dissolving 20 Gm. in 250 cc. of distilled water gives the plasma protein value of 1 pint of citrated blood. The administration of the dried plasma by dissolving it in double the quantity (500 cc.) of 5 per cent dextrose solution in distilled water, so that the fluid factor is increased for cases of shock, has been tried and found satisfactory. The ideal plasma for administration is group AB (1) plasma, but the plasma of any group may be given to any patient up to 500 cc. Group AB (1) plasma can be administered in any amount. Dried plasma can be stored at room temperature. It apparently remains effective indefinitely. The authors state that their experience is not great enough to assess the full value of the method, but its antishock property appears to be comparable to that of whole blood. It seems to be ideal for use in emergencies, when no supply of blood is easily available, and in war surgery. Its effects in wound shock and postoperative shock have been equal to those following a blood transfusion. In the treatment of severe burns and scalds their results confirm the already established claims of the efficiency of plasma infusions. In view of the possibilities of extensive demands being made on the resources of those who have to treat wound shock, the authors believe it imperative that any line of treatment claiming to be of value should be fully evaluated at the earliest opportunity.

1:425-470 (March 16) 1940

*Differential Diagnosis of Cushing's Syndrome (Basophilism) of Pituitary or Adrenal Origin. L. R. Broster.—p. 425.
Cardiac Examination in Wartime. J. Parkinson.—p. 428.
Emergency Preparation of Pyrogen-Free Water. J. C. Lees and G. A. Levvy.—p. 430.
Dental Anesthesia in Children: Comparison of Vinyl Ether and Ethyl Chloride in Series of 200 Cases. Jane O. French, M. L. Hooker, R. B. Vause and A. L. Robinson.—p. 432.
Inquiry into the Hour of Birth. Violet Spiller.—p. 435.

Cushing's Syndrome.—Broster compares Cushing's pituitary syndrome with the adrenogenital syndrome (adrenal virilism). There is a marked similarity in their mode of onset. In both there occur in a young woman an irregular growth of

hair of the male type and irregular menstruation. There is no absolute rule in the sequence of these two main symptoms. Either one or the other may occur first but sooner or later the two exist together during what seems to be a phase of definite endocrine instability. In Cushing's syndrome there develops a rapid and marked increase in adiposity, which becomes permanent and pathologic, followed by secondary symptoms (low sugar tolerance with or without glycosuria, raised blood pressure, erythrocythemia, cholesterolemia and coarse skin marked by striae). In adrenal virilism the weight usually remains stationary, but in some patients there is a definite increase, transitory and not excessive. None of the secondary symptoms of Cushing's syndrome appear. Instead of accumulating fat the patient becomes muscular and acquires secondary male characteristics. Between these two extremes there are many moderately heavy hairy women who cannot be labeled either with the Cushing's syndrome or with adrenal virilism. Two cases are cited which confirm the work of Crooke and Callow and further advances the role of the adrenal in basophilism. One of the two was a case of basophilism due to an adenoma of the pituitary with low urinary androgen, the other a case of basophilism due to adrenal hyperplasia with high urinary androgens reduced after the operation. The basophilic character of the growth was demonstrated by the ponceau fuchsin stain. In the case of basophilism due to adrenal cortical hyperplasia diagnosis was arrived at only by means of urinary assay for androgens. The immediate response to unilateral adrenalectomy, both clinically and biochemically, and the corroboration of the diagnosis by microscopic means, conform to the experience obtained on virilism. From the practical standpoint in the treatment of a condition which has heretofore been unsatisfactory and the study of his two cases, the author concludes that estimation of the urinary androgens affords a valuable means of making a differential diagnosis. When these are in excess it points to adrenocortical overactivity. Unilateral adrenalectomy in suitable cases offers a hope of alleviation, if not of cure.

Edinburgh Medical Journal

47:153-224 (March) 1940

Emergency Blood Transfusion Service. C. P. Stewart.—p. 153.
Migraine and Biliousness. D. M. Lyon.—p. 177.
Pathologic Significance of Intra-Articular Pressure. E. Freund.—p. 192.
Some Reflections on Two Recent Publications on Rickets. J. P. McGowan.—p. 204.

Journal of Mental Science, London

86:195-340 (March) 1940

Studies of Water Metabolism in Essential Epilepsy: I. Water Balance: II. Water Content of Blood. G. D. Greville and T. S. G. Jones, with technical assistance of W. F. G. Hughes.—p. 195.
Methodology in Psychologic Medicine. E. A. Bennet.—p. 230.
Use of Creatine-Creatinine Ratio. Caecilia E. M. Pugh.—p. 240.
Millon's Reaction in Urine of Mentally Defective Patients. Caecilia E. M. Pugh.—p. 244.
*Convulsion Therapy of Psychoses. A. M. Wyllie.—p. 248.
Anomalous Cardiac Occurrences During Cardiazol Treatment of Psychoses and Psychoneuroses. R. Good.—p. 260.
Brain Respiration and Glycolysis in Cardiazol Convulsions. L. D. MacLeod and M. Reiss.—p. 276.
Influence of Endocrines on Cerebral Circulation. M. Reiss and Yolande M. L. Golla.—p. 281.
Attempt to Induce Patients Suffering from Catatonia to Active and Voluntary Movements. J. Bierer.—p. 287.

Convulsion Therapy of Psychoses.—Wyllie reports on the results of convulsion therapy in 144 cases of various psychoses. The term "recovered" was used to indicate that all symptoms have disappeared, that some degree of insight has been restored and that the patient is fit to be discharged to home conditions and take up his former activities. The term "improved" indicated that a great change for the better has occurred in the patient's behavior and habits but that symptoms may remain and that insight has not been restored completely. Some of these patients are fit to be discharged from hospital care. Of fourteen patients in whom schizophrenia had existed for less than one year, seven recovered and six were improved, while only three of sixty-eight having the disorder for more than one year recovered. Although the number of early cases in his series is small, the author feels convinced that convulsion therapy is of definite value in the early treatment of schizophrenia. This is in harmony with the observations of most workers. Thirty-three of the sixty-eight patients were greatly improved. Of nine patients with paraphrenia of more than one year, none recovered but four improved. The results are similar to those in the chronic schizophrenic group. Patients in both the melancholic and the manic phases of manic-depressive psychosis responded immediately to the treatment. Of twenty-seven such patients treated, seventeen recovered and only one was unimproved. A happy feature was the rapid disappearance of suicidal tendencies. Of eleven patients with involutional melancholia who were ill less than two years prior to treatment, seven recovered. A considerable number of cases of involutional melancholia that would not recover spontaneously but would drift into chronicity could be saved by convulsion therapy. The average duration of illness of the patients who recovered (including one who was ill five years) was one year and two months, while the average duration of illness prior to treatment in the unrecovered group was five years and two months. Twenty-four patients in all were treated and of these eight recovered, eight were improved and eight were unimproved. The recovery rate from manic-depressive and involutional melancholias is not comparable with the spontaneous recovery rate. Only patients who did not show signs of recovery after a reasonable period were submitted to convulsive treatment. There were only two patients with psychoneurosis. The first, with obsessional neurosis, was greatly improved and the second, with hysteria, recovered. For involutional melancholia and the manic-depressive psychosis usually from two to seven convulsions were required to cut short the illness, while schizophrenic patients required a longer course. Relapses are common. The problem of how long to continue inducing convulsions and the success of the treatment rest on the physician's clinical intuition. If too few convulsions are induced, relapse is likely to follow, while continuance of the treatment after the maximal improvement has been attained subjects the patient to unnecessary risk and may be harmful.

Lancet, London

1:487-532 (March 16) 1940

Dosage of Sulfanilamide in Prophylaxis of Wound Infections. A. T. Fuller and G. V. James.—p. 487.
Treatment of Epilepsy with Sodium Diphenyl Hydantoinate. R. Coope and R. G. R. Burrows.—p. 490.
Hypophysis and Pancreatic Insulin. H. P. Marks and F. G. Young.—p. 493.
Acute Suppurative Parotitis: Treatment by Deep X-Ray Therapy. A. J. C. Latchmore, A. A. D. La Touche and H. S. Shucksmith.—p. 497.
Subdural Hematoma. W. L. Templeton.—p. 499.

Medical Journal of Australia, Sydney

1:253-288 (Feb. 24) 1940

Value of Femoral Osteotomy for Diseases and Injuries of Hip Joint. T. King.—p. 253.

1:289-324 (March 2) 1940

Acute Nephritis. A. J. Collins.—p. 289.
Hemolytic Streptococcus Infections Following Childbirth and Abortion: II. Clinical Features, with Special Reference to Infections Due to Streptococci of Groups Other Than A. A. M. Hill and Hildred M. Butler.—p. 293.
Some Aspects of Head Injuries. L. Lindon.—p. 299.
The Last Illness of Sir Henry Morgan, Kt., Buccaneer and Colonial Governor, as Described by His Physician, Sir Hans Sloane, Bart., When Resident in Jamaica, in the Years 1687 to 1688, and Some Account of the Latter's Subsequent Career. R. S. Skirving.—p. 302.

Practitioner, London

144:213-308 (March) 1940

Trends in Gastro-Enterology Today. W. C. Alvarez.—p. 213.
Some Observations on Gastric and Duodenal Ulceration. H. MacLean.—p. 222.
Difficulty in Swallowing. R. Coope.—p. 233.
Diseases of Small Intestine. T. C. Hunt.—p. 241.
Colitis. E. R. Cullinan.—p. 248.
Diet in Wartime. V. H. Mottram.—p. 258.
Some Problems of Evacuation as Experienced in a Midland County. F. D. M. Livingstone.—p. 268.
Anaphylaxis in Serum Therapy. C. E. Kellett.—p. 276.
Note on Amebic Infection from a Life Assurance Point of View. F. G. Cawston.—p. 282.
Modern Therapeutics: IX. Use and Abuse of Aperients. R. H. Micks.—p. 285.

Gazette des Hôpitaux, Paris

113:173-188 (March 6-9) 1940

*General Review of War Surgery. G. Jeanneney.—p. 177.

War Surgery.—Jeanneney discusses problems presented by extensive war injuries of the extremities with lacerations or contusions of the muscles and vessels, with fractured bones and open articulations; by crushed extremities that are cold and inert; by the wounded with multiple lesions, and by those who are in shock and almost moribund. War surgery requires a special organization: (1) advanced surgical posts, (2) centers of treatment that are subdivided according to specialties, (3) research centers charged with the study of the biology, pathologic anatomy and treatment of war wounds and (4) a service of surgical information. The basic ideas acquired during the Spanish war coincide with the author's own in that the latent time before deep infection of the war wound permits a prophylactic excision and, if necessary, a suture of the wound; the penetrating wounds of the cranium permit preoperative transportation; penetrating chest wounds, severe hemorrhage and shock do not permit transportation; the penetrating abdominal wound should be given priority in treatment. The following points are stressed: (1) lavage of the injuries only at the beginning, in order to remove the septic débris, (2) surgical cleansing of the wound, removal of foreign bodies and flattening of sinuous depressions, (3) antitetanic and antigangrenous therapy, (4) infrequent changing of dressings, even if the wound smells bad or changing only the cotton, leaving the wound itself untouched, thus avoiding unnecessary pain for the wounded, (5) supervising carefully the temperature and the general condition and (6) giving special attention to immobilization in a good position. Immobilization by a plaster of paris cast is recommended not only for fractures but also for wounds of the soft parts. The wounds are padded with petrolatum compresses and the dressings are changed at the end of two weeks. During the Spanish war closed plaster of paris casts were used for compound fractures, but the author thinks that this procedure should be used with prudence, because it involves the danger of "enclosing the wolf in the sheepfold." The pain of the amputation stump has been known to respond to daily injections of vitamin B. Tetanus is best controlled by antitetanic vaccination, which may be combined with antidiphtheric and antityphoid vaccination. In a wounded person who has been vaccinated it will be sufficient to give one injection in order to increase the defensive power of the organism. In the nonvaccinated wounded it is necessary to inject as soon as possible 1 cc. of vaccine and forty-eight hours later 3,000 units of antitoxin. Two other injections of vaccine should be given at intervals of three weeks in order to confer an immunity of at least two years' duration. Ramon's antitetanic vaccination consists of three subcutaneous injections of toxoid (1, 2 and 2 cc.) given at intervals of three weeks, and a year later 2 cc. is injected. The same technic is employed in case of combined vaccinations with mixed vaccines. When a correctly vaccinated subject sustains a tetanigenic injury he should be given an injection of tetanic toxoid so as to augment the immunity without exposing him to possible complications from serum. If doubt exists as to whether a wounded person has been vaccinated or, if the wounds are multiple and have caused severe hemorrhages, it is best to combine the injection of toxoid with serum treatment. If tetanus is developing, serotoxoid therapy should be employed.

Progrès Médical, Paris

68:161-208 (March 2) 1940. **Partial Index**

*Pathologic Physiology of Frostbites: Vasomotor and Thrombotic Disease. R. Leriche and J. Kunlin.—p. 169.
Grave Acute Tetanus: Serotoxoid Therapy; Cure. J. Minet and Bertrand.—p. 178.
Dyspepsias of Tuberculous Patients. M. Loeper.—p. 182.
Cardiac Disturbances in Progressive Posthemorrhagic Anemias. G. Marchal.—p. 191.

Frostbites, a Vasomotor and Thrombotic Disease.—Leriche and Kunlin treated thirty-nine cases of frostbite. In six the hands were involved and in thirty-three the feet. The cold produces first a vasoconstriction, which after a certain period becomes pathogenic, producing anesthesia and analgesia. When the footwear or the gloves are taken off, usually in a warm atmosphere, vasodilatation takes place. Later large blisters appear in the zone of vasodilatation. The fluid within these vesicles is at first clear but quickly becomes hemorrhagic. The nails become raised and eventually fall off. In about half of the observed cases this phenomenon extended to all toes or fingers; but on the feet it was sometimes only one toe, the great one, whereas on the hands the thumb remained intact five times out of six. In the zones in which blisters do not develop, a violet-black coloration appears; the skin becomes withered and insensitive and it is evident that dry gangrene is developing. In this phase the frozen foot presents three aspects: a tarsal zone of red edema, a metatarsal zone of yellow blisters and a peripheral zone (toes) of dark violet discoloration. Arteriography discloses obliteration in cases of frostbite. The cicatrized skin remains sensitive and painful for many years. The process is not completely terminated with the disappearance of the edema and the completion of cicatrization. The authors believe that these patients retain arteritic lesions. They observed that two patients who sustained frostbites in 1917 presented intermittent claudication and pains of the arteritic type in 1935. Anesthetic infiltration of the lumbar and stellate sympathetic was the treatment to which they resorted in all frostbite patients with edema and pain. Nearly all were immediately relieved. The infiltrations were repeated on the following two days. It was found that, if there was no necrosis or infarction, all was well in a few days. They conclude that anesthetic infiltration of the sympathetic is the best mode of treatment for frostbite and chilblains. The authors hope that this simple treatment will find wide application, since the customary treatments prevent neither the pain nor the gangrene.

Riforma Medica, Naples

56:165-200 (Feb. 10) 1940

*Blood Transfusion in Leukemia. F. Corelli and M. Gaetano.—p. 167.
Oriel's P. Substance in Urine After Surgical Operations. L. Imperati.—p. 175.

Blood Transfusion in Leukemia.—Corelli and Gaetano gave repeated blood transfusions to nine patients with chronic myeloid or lymphatic leukemia. In addition, roentgen therapy was given in the majority of the cases. The amount of blood for each transfusion varied from 200 to 300 cc. The number of transfusions, the intervals and the duration of the treatment were determined by the course of the disease. Repeated blood transfusions alone brought about improvement in the general condition of the patients. The blood picture was not modified. Both the latter and the former were improved by transfusion combined with roentgen therapy. The combined treatment gave better results than roentgen treatment alone. All the patients were followed up. Improvement was moderate. In one grave case it was transient. Two patients lived in a satisfactory condition for eight months after discontinuance of treatment. Two other patients lived in a satisfactory condition for two and four years, respectively. They developed fatal bronchopneumonia. Four patients are alive and in a satisfactory condition at the present (from eight months to four years after discontinuance of the treatment). Two of the patients resumed work. The patient living four years after discontinuance of the treatment is the only one to have an occasional blood transfusion.

Rivista di Patologia e Clin. d. Tubercolosi, Bologna

14:69-136 (Feb. 29) 1940. **Partial Index**

Syphilis in Tuberculous Patients. M. Valli.—p. 69.
*Digitalis in Emetic Cough in Pulmonary Tuberculosis. A. Iraci.—p. 102.

Digitalis in Cough with Vomiting in Pulmonary Tuberculosis.—Iraci believes that cough with vomiting in pulmonary tuberculosis is caused by circulatory disorders due to latent insufficiency of the heart. He administered digitalis to twenty-five patients with chronic pulmonary tuberculosis in whom various forms of therapy failed to control emetic cough. The drug was given intramuscularly during six consecutive days: three daily injections for the first two days, two daily injections for the next two days and one daily injection for the

last two days. Cough was controlled in fifteen cases. In two it recurred after a period of from one to seven months after treatment was discontinued. It was controlled by repeated administration of digitalis. The results of the treatment were mediocre in two cases and failed in eight, among which were two cases of laryngeal tuberculosis.

Brasil-Medico, Rio de Janeiro

54:1-16 (Jan. 6) 1940. **Partial Index**

*Treatment of Tetanus of the Newborn. A. Ferrari.—p. 1.
Spontaneous Aneurysm of Subclavian Artery: Case. J. Adonias Aguiar and M. F. Vieira Lima.—p. 2.

Treatment of Tetanus in Newborn Infants.—According to Ferrari, failure of antitetanic serum when administered alone in the treatment of tetanus of the newborn is due to acidosis, functional and hepatic disturbances and the upsets in the acid-base balance which take place in the course of tetanus. Other treatment besides the serum is needed. The patient is kept at complete rest in a quiet room away from noises. In the first few days, in addition to the local treatment, the patient is given five enemas of 60 cc. each of a solution containing 100 Gm. of dextrose, 1 liter of boiled water and 50 Gm. of sodium bicarbonate. The enemas are given at intervals of three hours, after which the patient is permitted to rest. The local treatment consists of applying small pledgets of cotton moistened in diluted solution of sodium hypochlorite to the navel and the skin around the umbilical scar, using each swab only once, after which five drops of a 2 per cent solution of silver nitrate (freshly prepared) are dropped on the navel and the latter is dressed with dry gauze and a protective bandage. The sodium bicarbonate-dextrose enema possesses detoxicating and nutritional properties. Feeding by mouth during the acute phase of tetanus is entirely prohibited. It may cause pharyngeal, laryngeal or esophageal spasm and acute asphyxia. It is recommenced after the complete subsidence of the tetanic crises.

Revista de la Assoc. Méd. Argentina, Buenos Aires

54:1-64 (Jan. 15-30) 1940. **Partial Index**

Latent Cancer of Lung with Early Clinical Symptoms of Bone Metastases and Sciatic Syndrome: Cases. M. R. Castex, E. S. Mazzei and M. S. Dreyer.—p. 1.
*Antiemetic Properties of Magnesium Sulfate. R. L. Repetto and L. E. Camponovo.—p. 35.

Antiemetic Properties of Magnesium Sulfate.—Repetto and Camponovo report satisfactory results from the administration of magnesium sulfate in the treatment of vomiting. The authors carried out experiments on dogs and observations on twelve patients in a psychopathic institution. Patients and animals were given an intramuscular injection of from 5 to 10 cc. of a 25 per cent solution of magnesium sulfate, five or ten minutes before or simultaneously with the administration of apomorphine hydrochloride. The latter was administered subcutaneously to patients in doses of 0.005 Gm. of apomorphine and to the animals in doses of from 0.001 to 0.005 Gm. of the drug by the intramuscular route. A group of patients were given ipecac instead of apomorphine in three cachets, each containing 0.5 Gm., at intervals of five minutes. The authors found that the effects of the drug are manifest in from ten to twenty minutes after its intramuscular administration. The effective dose for man varies from 5 to 10 cc. of the 25 per cent solution of magnesium sulfate in distilled water given intramuscularly. The dose can be repeated the same day, not to exceed the total daily dose of 20 cc. The treatment is indicated in all cases of spontaneous vomiting and that complicating various diseases, especially in the presence of pain, insomnia and neuromuscular excitability. Magnesium sulfate is the only substance capable of neutralizing the emetic effects of apomorphine. It acts by diminishing the excitability of the bulbar centers of vomiting. The authors did not observe a depressive effect of the drug on the respiratory centers. Theoretically an intravenous injection of calcium can be resorted to because of its antidotal action for magnesium sulfate, along with the administration of drugs capable of stimulating the centers of respiration.

Archiv für Kreislaufforschung, Dresden

6:1-108 (Jan.) 1940. **Partial Index**

Cardiopneumatic Movement, Its Form, Nature and Its Behavior in Low Pressure Regions: Relation of Cardiopneumatic Movement to Arterial Pulse. E. M. Müller and H. O. Wachsmuth.—p. 1.
Experimental Changes of Quantity of Blood: Behavior of Basal Metabolism During Withdrawal of Blood. H. Brüner and K. H. Butzengeiger.—p. 34.
Criticism of Theory of Pathogenesis of Attacks of Bronchial Asthma on Basis of Disturbance in Pulmonary Circulation. M. Takino and S. Okada.—p. 47.
Significance of Pressure Amplitude and of Cardiac Reflex for Reflex Autoregulation of Circulation. E. Strauss.—p. 65.
Increase in Action Tension Curve of Ventricle. M. Decker.—p. 75.
*Pathologic Aspects of Electrocardiograms Taken During Exertion Tests and Their Clinical Significance. P. Laurentius.—p. 83.
Basal Metabolism After Exclusion of Pressure Receptors. W. Hahn.—p. 97.

Significance of Changes in Electrocardiogram Taken During Exertion Tests.—Laurentius made electrocardiographic studies on 150 persons. Thirty per cent of these presented pathologic conditions of the heart (valvular lesions, previous endocarditis or hypertension) without signs of decompensation. In an additional 30 per cent the existence of subjective cardiac symptoms suggested a latent myocardial or coronary insufficiency. In this group the author included all who complained of symptoms suggestive of angina pectoris. The remaining third included persons who had palpitation, vertigo, fainting, shortness of breath on exertion, arrhythmia and decrease in the functional capacity. Eighteen of this last group had a myocarditis (complication of scarlet fever, diphtheria and tonsillitis) from six months to three years previously. This group also included patients with obesity, exophthalmic goiter, Werlhof's disease, benzene poisoning and nicotine poisoning. In cases in which anomalies were detected in the electrocardiogram taken at rest, the exertion test was omitted. In the presence of slight changes, the tolerance test was made in order to clarify the doubtful changes. The exertion test consisted in ascending a stairway of twenty steps two or three times. From three to five electrocardiograms were taken in each case. In 52 per cent the electrocardiograms taken after exertion were normal, but in the remaining 48 per cent disturbances were noticeable in the formation of the impulse and in the conduction. Changes in the final deflection, indicative of myocardial impairment, were observable in 28 per cent. It was thus demonstrated that in the absence of decompensation and with a normal electrocardiographic record taken at rest the exertion electrocardiogram may reveal pathologic changes. For an exact evaluation of the circulatory organs, several methods of examination must be employed. The exertion electrocardiogram is only one of several methods by which latent cardiac defects can be brought to light. It is not a universal and independent functional test of the heart.

Beiträge zur klinischen Chirurgie, Berlin

170:513-664 (Dec. 31) 1939

*Modifications in Secretions of Gastric Juice in Gallstone Diseases Before and After Extirpation of Gallbladder. L. von Murányi.—p. 513.
Syphilitic Soft Tumors of Mammary Gland (Gumma Mammae). K. Hollósi.—p. 540.
Radical Operations of Carcinomas of Papilla. W. Kafka.—p. 547.
Local Anesthesia in Major Surgical Cases. F. Osswald.—p. 560.

Modifications in Secretion of Gastric Juice in Gallstone Diseases.—Von Murányi employed Einhorn's fractionated breakfast test and duodenal tube in sixty-four cases of gallstone disease. There were eleven men and fifty-three women between the ages of 20 and 50 years who had been examined preoperatively, kept on a postoperative dietary regimen for at least a year and reexamined. The sixty-four cases fell into four groups: simple gallstones twenty-six (40.6 per cent), with occlusion of bile ducts twenty-one (32.8 per cent), with icterus five (7.8 per cent) and with acute cholecystitis twelve (18.8 per cent). The tests had the threefold objective of determining (1) whether characteristic acidity curves could be obtained, permitting prompt and sure diagnosis of gallstone involvement, (2) whether the majority of gallstone cases were characterized by achylia or hypo-acidity and (3) whether gallbladder extirpations modified gastric secretions inducing dyspepsia. The results diverge widely from assumptions held at present. In only seven

cases of the twelve belonging to the acute cholecystitis group did the acidity curves indicate approximately uniform results. Great individual differences were found. The author summarizes this portion of his investigation by saying that no secretion curves of gastric acidity peculiarly significant for gallstone diseases and useful for differential diagnosis could be attained. Achylia or hypo-acidity was found in only eighteen cases (28.2 per cent). Analyzed according to their group membership, five (7.8 per cent) of the twenty-one cases were complicated with occlusion of the bile ducts, one (8.3 per cent) of twelve cases was complicated with icterus and eight (21.7 per cent) of the twenty-six uncomplicated gallstone cases manifested hypo-acidity. His observations, therefore, do not sustain the assumption that gallstone disease, complicated or uncomplicated, develops subacidity in 66 per cent of the cases. Gallbladder extirpation not only had no adverse effect on gastric secretion but stimulated a tendency to return to normal levels in almost all cases. Achylia or hypo-acidity observed preoperatively in 28.2 per cent of the cases was present after the operation in 15.6 per cent. Hyperacidity was reduced from an incidence of 29.6 per cent to that of 12.5 per cent, and normal values, found in 42.2 per cent, were increased to 71.9 per cent. The author comments on the difference of results obtained by the Einhorn fractionated test from those of the Boas-Ewald single test. Neither sex nor age (limited to age 50) was found to affect the chemical modifications of gastric secretion. He believes that postoperative freedom from dyspepsia is determined by the strict observance of a dietary regimen for at least a year.

Deutsches Archiv für klinische Medizin, Berlin

185:273-392 (Nov. 28) 1939. **Partial Index**

Blood Picture Changes in Lymphogranulomatosis. A. Gebauer.—p. 273.
Heart Injuries in Carbon Monoxide Poisoning. G. W. Parade and H. Franke.—p. 294.
Significance of Mixed Infection of Tuberculosis Cavities with Streptococci. W. Übelacker.—p. 303.
Acute Isolated Lymphogranulomatosis of Spleen: Case. A. Gebauer.—p. 339.
Insulins with Retarded Action in Persons with Normal Metabolism. K. Mellinghoff and G. Voges.—p. 345.
*Cases of Chronic Nephrosis and Pseudonephrosis at the Volhard Clinic (1918 to 1938). Erika Oertel.—p. 357.

Chronic Nephrosis and Pseudonephrosis.—Oertel made a comparative analysis of fifty-nine cases of chronic nephrosis and thirty-one cases of pseudonephrosis. She points out that chronic nephrosis occurs as a result of a primary increase of albumin transmissibility of the glomeruli caused by toxic action, while pseudonephrosis occurs as a result of a secondary or indirect increase of albumin transmissibility of the glomeruli caused by circulatory disturbance of the glomeruli. In attempting differential diagnosis, one should carefully analyze the history and the course of the disease. The significance of blood pressure behavior is also stressed. The differential diagnosis is made increasingly difficult at times by overlapping symptoms and the apparent similarity of pathologic-anatomic and microscopic observations. Pseudonephrosis is, as a rule, incurable, while true cases of chronic nephrosis often are curable.

Deutsche medizinische Wochenschrift, Leipzig

66:113-140 (Feb. 2) 1940

Serotherapy of Acute Pneumonia. G. Wiele and H. Ibeling.—p. 113.
Course of Lobar Pneumonia in Adults. Frobenius.—p. 118.
Pneumonia Complicating Influenza. H. Dennig.—p. 122.
*Treatment of Bronchial Asthma with Minimal Doses of Copper. G. Schimert.—p. 124.
Prepellagral Conditions. A. Mahlo.—p. 126.
Circulatory Insufficiency. R. Klotz.—p. 128.
Early Bacteriologic Diagnosis of Abdominal Typhoid. F. Lommel.—p. 130.

Small Doses of Copper in Bronchial Asthma.—The fact that heavy metals administered in small doses increase the activity of the reticulo-endothelial system and thereby influence the allergic condition suggested to Schimert the rationale of treating bronchial asthma with small doses of copper. He chose copper because its oral administration has been found helpful in spasmodic conditions of the smooth muscles, particularly the bronchial muscles. In the majority of cases the cutaneous administration of 10 micrograms of colloidal copper twice weekly proved most effective after the initial reaction had subsided. In some the weekly dose had to be reduced to 1 or 2 micrograms and in others it had to be increased to from 50 to 100 micrograms. The treatment was begun with a subcutaneous injection of 0.5 cc. (containing 5 micrograms). If no severe reactions followed (in the form of greater frequency and intensity of attacks), the same dose was given three days later by intravenous injection. If the attacks were intensified, the subcutaneous injection was resumed. It was possible, as a rule, to establish the intravenous mode of injection at the sixth or eighth injection. At this time it was also possible to increase the dose to 1 cc. The initial exacerbation should not be regarded as a reason for abandoning the treatment, for after twelve to twenty days improvement sets in as a rule. The treatment is continued for from six weeks to six months. It is advisable to continue the injections for some time after the cessation of the attacks. In some cases the injections must be continued at ten day intervals in order to maintain the patient free from symptoms. The author reports observations on fifty patients, twenty-one of whom were completely freed from attacks, seventeen were greatly improved, five had relapses and seven were not improved.

Monatsschrift für Kinderheilkunde, Berlin

81:281-398 (Feb. 8) 1940. **Partial Index**

Anaphylaxis and Hepatic Function. J. Recht and F. Gerióczy.—p. 281.
Theoretical and Practical Remarks on Fluid Treatment in Conditions of Exsiccation. E. Kerpel-Fronius.—p. 294.
Studies on Vaccination: Vaccination Against Smallpox as Allergic Reaction. D. Gyüre.—p. 305.
*Transfusion of Large Quantities of Plasma in Toxicosis of Infants. F. H. Dost.—p. 312.
Feeding of Prematurely Born Infants. W. Catel.—p. 334.
Calory Requirements of Prematurely Born Infants. H. Knauer.—p. 372.

Transfusion of Plasma in Toxicosis of Infants.—According to Dost, surprisingly favorable results were obtained by Bessau and Uhse with transfusion of plasma in infants with toxicosis due to dyspepsia. Dost applied this treatment in eleven cases during the subtoxic or toxic stage. In severe diarrhea without toxic disturbances he considered it unnecessary to depart from the customary treatment. No children after the first year of life were included. He was unable to corroborate the favorable results reported by Bessau and Uhse. The loss of water was rapidly compensated and the remissions were sudden but as a rule of only short duration. Cure was obtained in only two of the eleven cases. The favorable results were overshadowed by complications. In two instances transfusion was followed by circulatory impairment, apnea and death. In another case death followed after 28 cc. of plasma per kilogram of body weight had been given, although the total dose is 50 cc. per kilogram of weight. Intestinal peristalsis increased during or after the transfusion and watery stools were eliminated. Apparently the organism tries to rid itself of part of the excess of fluid by intestinal elimination. The signs of severe collapse may be due to the excess load imposed on the circulation. In four cases which terminated in death, signs of endocarditis simplex were observed which the author ascribes to the plasma transfusion.

Münchener medizinische Wochenschrift, Munich

87:57-84 (Jan. 19) 1940. **Partial Index**

Results of Roentgen Therapy in Malignant Tumors of Supramaxillary Region with Special Consideration of Their Ophthalmologic Involvement. H. T. Schreus and F. K. Leydhecker.—p. 62.
Disease-Producing Viruses. P. Heilmann.—p. 64.
*Treatment of Mixed Type Pneumonias with Combined Quinine Urethane and P-Aminophenylsulfonamide (Azosulfamide). H. Leonhardt.—p. 66.
An X-Ray Screen Apparatus for Clinical Use. K. L. Schmidt.—p. 68.

Treatment of Mixed Type Pneumonia with Combined Quinine Urethane and P-Aminophenylsulfonamide (Azosulfamide).—Leonhardt reports the successful use of combined quinine urethane and p-aminophenylsulfonamide in fifty cases of pneumonia during the course of four months. Forty were mixed type cases, mostly bronchopneumonia. The remaining ten were lobar pneumonia, three of which belonged to a mixed type. Five cases are reported. In the three bronchopneumonic cases (ages 22 to 80) streptococci and pneumococci were found, respectively, of types I, II and III. Consolidation was detected

either in one or in both inferior lobes. The combination drug was administered intramuscularly daily in doses of 1 or 2 cc. for from three to four days with significant therapeutic response in terms of fever subsidence and resolution of consolidation. One of the patients, aged 38, with lobar pneumonia, after unavailing preceding medication with other drugs, contracted a septic mixed type pneumonia which yielded promptly to the combination. The author's procedure with adults consisted of intramuscular administration of 2 cc. once or twice daily according to the severity of the case (half dose to children). Intramuscular treatment was followed, after defervescence, with oral doses of the same drug in tablet form. In no case were intolerance or untoward sequels observed even when the drug was given for seventeen days and totaled 68 cc. for a patient aged 69. In bronchopneumonia therapeutic effects were surprisingly rapid, a change for the better being noted within twenty-four to forty hours, together with a rapid resolution of local consolidation. The drug was applied successfully in postoperative cases as a prophylactic measure. Recurrences due to premature discontinuance were quickly checked by restoring medication. The same favorable results were obtained in lobar pneumonia. Neither postpneumonic empyemas nor complications attributable to the use of the drug were observed. The two deaths noted by the author in lobar pneumonia were due either to pulmonary embolism or to circulatory insufficiency that occurred after defervescence had already set in. The author thinks that the combination of the two drugs used in these cases can be successfully applied to all types of pneumonia.

Zeitschrift f. d. ges. experimentelle Medizin, Berlin

107:1-160 (Dec. 9) 1939. **Partial Index**

Chemical Constitution and Therapeutic Action of Various Calcium Compounds. A. Lassner.—p. 1.
*Treatment of Hemorrhagic Diatheses: Clinical Significance of Landis' Method. L. Armentano.—p. 9.
*Experimental Studies on Behavior of Anesthesia at Different Times During the Twenty-four Hour Period. Y. Edlund and H. Holmgren. —p. 26.
Investigations on Rest Nitrogen of Blood and Its Chief Components. P. Larizza.—p. 53.
Determination of Cutaneous Temperatures on Men Over 60 Years of Age. F. König.—p. 98.
Thyroid and Nutrition in Regions with Few Goiters and with Many Goiters. W. Bergfeld.—p. 106.

Treatment of Hemorrhagic Diatheses. — Armentano's studies failed to corroborate observations of other investigators that vitamin C is effective in various hemorrhagic disorders. He employed Landis's method in order to detect cases of increased capillary permeability. Cases with increased permeability were treated with vitamin C or citrin, the flavone fraction of lemon juice. Vitamin C proved ineffective in various chronic hemorrhagic diatheses, such as hemophilia, thrombopenia and vascular purpura. In symptomatic hemorrhages the treatment with ascorbic acid was successful only when a considerable deficiency of vitamin C existed simultaneously. Such a deficit of saturation could be demonstrated in eight cases: one of hemophilia, two of vascular purpura and five of essential thrombopenia. The Landis method is applicable in clinical examination for the permeability of the capillaries. In serous inflammations, effusion of plasma fluid as well as of protein can be observed. The same is true of cases of vascular purpura and nephroses. Citrin, the flavone fraction of lemon juice, arrests hemorrhages, increases the capillary resistance and prevents the effusion of protein from the capillaries only in vascular purpura but not in the other types of hemorrhagic diathesis. In hemophilia, thrombopenic purpura and panmyelophthisis, citrin proved to be entirely ineffective. The number of thrombocytes and the coagulation time are not influenced either by citrin or by vitamin C.

Anesthesia at Different Times During Twenty-Four Hour Period.—Edlund and Holmgren maintain that the liver has an important part in the detoxication of anesthetics. Reports in the literature indicate that this process of detoxication can be inhibited by starvation, cachexia and adrenalectomy. Attempts have been made to modify the chemical processes of detoxication by the administration of dextrose, glycogen, insulin and thyroxine. It has been demonstrated that the glycogen content of the liver varies rhythmically in the course of the twenty-four hour period, the maximum being reached during the late night and early morning hours and a minimum about 11 a. m. A number of male white mice were anesthetized with avertin with amylene hydrate at 6 a. m. and a number at 11 a. m. The authors found that the animals anesthetized at 6 a. m. showed a greater resistance than those anesthetized at 11 a. m. The second series of experiments were made with evipal soluble. Here again the mice subjected to anesthesia at 6 a. m. displayed a greater resistance than those subjected to it at 11 a. m. The authors investigated the effect of starvation and of insulin plus dextrose. Observations on animals treated with insulin and dextrose indicated that such animals had a greater resistance to the anesthetic than animals which were starved before anesthesia. An impression was gained that a certain parallelism exists between the time required for the anesthetic to take effect and the glycogen content of the liver. The authors conclude that a certain parallelism exists between the function of the liver and the rapidity, depth and length of the anesthesia.

Vrachebnoe Delo, Kharkov

21:451-530 (Nos. 7-8) 1939. **Partial Index**

*Lactic Acid Therapy of Cardiac Patients. E. Ya. Sterkin, P. F. Lomakin, N. A. Sulimovskaya, A. T. Lomen and E. M. Ylitskaya. —p. 451.
Combination of Symptoms of Decompensation in Cardiovascular Diseases. M. V. Burgsdorf.—p. 457.

Lactic Acid Therapy of Cardiac Patients.—According to Sterkin and his co-workers there exist sufficient experimental data to suggest that lactic acid, more so than dextrose, acts as a source of energy for the heart muscle and that it is capable of increasing the work capacity of the myocardium. The possibility of treating cardiac patients by increasing the blood lactic acid concentration presented itself. The authors have demonstrated that this can be accomplished by oral administration of a solution of invert sugar, a mixture of various quantities of dextrose and fructose. The method has the advantage over the method of work hyperlactacidemia in that it does not place additional burden on the heart. Another advantage is that invert sugar is converted to the D form of lactic acid necessary for the human organism. Studies on twenty-five patients with decompensated hearts demonstrated that the lactic acid blood content at rest and on a fasting stomach is frequently increased above normal. After administration of invert sugar a further increase in concentration takes place, so that sixty minutes after ingestion the lactic acid blood level exceeds the original level by from 50 to 60 per cent. The consequent lowering of the lactic acid blood level is, as a rule, retarded so that the level two hours after ingestion is still above the original. These observations, the authors believe, suggest the administration of invert sugar as a source of lactic acid in the treatment of cardiac patients.

Nordisk Medicin, Gothenburg

5:165-198 (Feb. 3) 1940. **Partial Index**

Hospitalstidende

*Peculiar Case of Nephrosis. K. O. Høegh.—p. 169.
Lesions of Recurrent Nerve in Thyroidectomy in Exophthalmic Goiter. P. Winfeld.—p. 174.
Creatinuria and Cholesterolemia in Castrates. K. Brøchner-Mortensen. —p. 180.

Peculiar Case of Nephrosis.—A man aged 25, with active pulmonary tuberculosis and chronic tuberculosis of the bones, contracted nephrosis immediately after thoracoplasty done about six months before death. Høegh ascribes the nephrosis to the effect of toxins from the tuberculous process. He says that the case differs from our known cases of tuberculous nephrosis in that there was an extremely high albuminuria together with marked edema. Tuberculous nephrosis is considered incurable, as it is maintained by the primary disorder, but in this instance the albuminuria disappeared after about four months, and somewhat later, without change in the serum proteins or the estimated colloid-osmotic pressure, the edema disappeared, presumably because of variations in the hydrostatic pressure. Necropsy showed no hyaline or amyloid degeneration of the kidneys, but there was pronounced albuminous degeneration, especially of the tubuli contorti.